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BIOTECHNOLOGY

OPPORTUNITIES FOR INNOVATION

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Opportunities for Innovation: Biotechnology

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FOREWORD

At the National Institute of Standards and Technology (NIST), we strive to promote U.S. economic growth by working with industry to develop and apply technology, measurements, and standards. We have a variety of mechanisms—some old, some new—to meet many kinds of industry needs.

NIST laboratory researchers work with industry to develop new techniques; devise new measurement methods; and provide materials, data, and calibrations for quality assurance. The Malcolm Baldrige National Quality Award, which NIST manages with the private sector, recognizes companies for improvements in quality management.

Other NIST programs are designed to spur innovation and accelerate the adoption of new ideas and technology by U.S. companies. For example, through the Advanced Technology Program, we help companies share the cost of high-risk research with broad commercial potential. In addition, we are building a Manufacturing Extension Partnership to assist small and medium-sized manufacturers in modernizing their production capabilities.

By promoting strategic partnerships between small and medium-sized technology-based companies and large manufacturing corporations, the NIST Opportunities for Innovation Program aims to facilitate and accelerate the commercialization of technology. Through regional workshops and monographs like this one, the OFI Program stimulates the vital exchange of information among companies.

According to G. Steven Burrill in *Biotechnology Business* (Ernst & Young, 1993), strategic partnerships between biotechnology companies have proved to be, in most cases, a "win-win" structural arrangement for both partners. Strategic partnerships promise to spur the formation of "virtual enterprises" in a broad spectrum of functions, including research and development of new products.

The majority of companies, however, do not participate in this process fully because of their limited human and material resources. Therefore, small firms that are engaged in developing and marketing a single product or a limited line of products are often not aware of the many opportunities that exist outside their main line of business. And yet, because small companies frequently have tremendous enthusiasm, entrepreneurial spirit, motivation, and intellectual capital, they could increase their spectrum of new products given the opportunity. At the same time, small entrepreneurial companies often represent a resource of niche technologies that large corporations could help commercialize and market worldwide.

This monograph, *Opportunities for Innovation in Biotechnology*, was conceived with the needs of a small company in mind. It provides the technical staff of a small firm with a multi-company report on the best opportunities for new business endeavors in a technology-driven market.

Each chapter of the monograph, written by an expert in the field, focuses on one specific issue of biotechnology where new technical advances hold promise of early commercialization and entry into a new market. The authors point out the barriers and shortcomings in current, state-of-the-art practice that prevent the commercialization of the current technological knowledge and that represent an opportunity for a small firm.

Using the technological information in this monograph as a basis, we plan to hold a series of regional workshops that will include both small companies and large manufacturers. The workshops also will provide discussions on business opportunities and the availability of financial and material resources.

The OFI Program has already produced monographs and workshops dealing with polymer composites, a fast evolving technology finding wide applications in the automobile, aerospace, and consumer goods markets; chemical and biological sensors for the chemical and processing, automotive and power-generating, and health care industries; and advanced manufacturing technology that addresses the needs of small to medium-sized firms engaged in the manufacturing of discrete parts.

It is by improving the flow of technological information and encouraging the formation of strategic industrial partnerships that we hope to help U.S. companies accelerate commercialization of technological advances.

Arati Prabhakar
Director, NIST

PREFACE

This monograph in the "Opportunities for Innovation" series deals with biotechnology, a mature but explosive technology finding a rebirth in the discoveries of the structure of DNA and RNA that led to the development of advanced techniques for selectively altering the genetic makeup of cells though genetic engineering, development of monoclonal antibodies and hybridomas, and somaclonal variation of plant cells.

Biotechnology is being viewed by many as one of the major technological opportunities of this century ranking with the explosive growth of telecommunications, computers, and space exploration. Certainly the rush to participate by conservative established companies, new startup companies, investors, university scientists, governments, international organizations, and the media support this view. Expectations for the new biotechnology are very high. Whether such expectations will be completely realized is another matter. However, the flow of resources—money and trained scientific personnel—over the past decade into this new research area suggests that such prophecies may become self-fulfilling.

In general, biotechnology can be expected to have a major impact on fundamental human needs engendered in the market segments of: health care, agriculture, forestry, food ingredients, industrial chemicals, plastics, energy, mining, pollution control, and bioelectronics. At present, innovations in health care aimed at very high value-in-use therapeutic proteins are in the forefront with crop agriculture a far second. Innovations in pollution control are coming up strong as a result of increased public and regulatory pressure. However the interest in biological approaches to commodity chemicals based on renewable raw materials has waned as a result of the continued softness in crude oil prices.

Certainly the commercial stakes are high. Biopharmaceuticals, that reached U.S. sales levels of $2.4 billion in 1992, are forecast to reach $9.3 billion by 2002 among the market segments: cancer— $2.9 billion, cardiovascular—$2.1 billion, vaccines—$1.9 billion and hormones and growth factors—$1.8 billion. In addition, sales of diagnostics are expected to reach $2.5 billion from a current level of $1.0 billion.

Agricultural biotechnology, which has lagged health care in delivering new products, is expectantly poised for a growth rate of 35% per year with sales rising from $70 million in 1992 to over $1 billion by 2000.

About 97% of the current market for synthetic organic chemicals is technically, if not economically, vulnerable to replacement by bio-derived counterparts. This potential conversion amounts to 5 billion pounds of specialty chemicals valued at an average price of $1 per pound and 311 billion pounds of commodity chemicals valued at $108 billion. Thermoplastic polymers have an additional market potential for biopolymers of 51 billion pounds.

Opportunities for bioproducts as food ingredients amount to $1.76 billion in functional additives, $1.1 billion in non-nutritive sweeteners, and $300 million on fat replacers.

The EPA estimates that the cost of federally mandated pollution control and cleanup reached $115 billion in 1990. Continued public and regulatory pressure will promote the expansion of bioremediation. The use of indigenous bacteria and imported microbes to clean up contaminated soil and ground water is expected to grow at a rate of 20-30% in the 1990's—virtually regardless of prevailing economic conditions.

Likewise, the strict requirements of the Clean Air Act will create a market for the microbial desulfurization of coal by as much as $50 billion by 2000. The Act is also expected to expand the market for bioethanol as an octane enhancer in gasoline.

Similarly, chemically-treated bacteria, chitin, carrageenan, modified cellulosic wastes, and starch xanthate are all serious contenders in the market for the biological recovery of metals, expected to top $500 million in the United States by 2000.

The basic purpose of this project is to help small businesses get on the fast track in biotechnology research and development leading to the spin off of viable commercial businesses, probably with the help of larger companies having the resources for commercialization that are lacking in a small enterprise. Such resources could include financing, and positions in marketing, manufacturing, regulatory affairs, and raw material supply, to name a few.

PREFACE (continued)

This does not mean, however, that the objective of the monograph is restricted to providing the businessman with an immediate opportunity to apply biotechnology profitably. Indeed, commercialization may be many years away and the business catalyst might be the merger of organizational resources at a critical time in the research program. Almost all of the much heralded coalitions in human health care have occurred in this way.

A multifaceted approach has been taken in designing the monograph so as to include:

- Research on new products, even at the bench scale, based on a scientific discovery that if translatable to commercial scale would be assured of market acceptance. Pharmaceuticals for human or animal health care and plant growth regulators for agriculture would be examples of this category.
- Research on new or improved processes for producing existing products having commercially relevant objectives for scale up to viable businesses providing a competitive cost advantage over the incumbent processes. Certain speciality chemicals such as lactic acid and citric acid and commodity chemicals as ethanol and acetone/butanol are examples of this.
- Research on products or services mandated by legislation to alleviate the adverse effects of pollution in its various forms. Examples include: bioremediation, bioprocessing of minerals, biodegradable plastic packaging materials, algae systems for removing carbon dioxide from flue gas, etc.
- Research on products based on coal or renewable natural resources which, although at a current competitive cost disadvantage compared with products from petroleum feedstocks, have a strategic importance to the United States in the event of disruptions of international trade. Examples include ethanol, biogas, polymers for enhanced oil recovery, conversion of coal to liquid or gaseous fuels, etc.

In spite of the positive side of new bioproducts, the businessman must also be aware and prepared to deal with some cases in which a biotechnology solution to a particular problem creates additional problems, be they of technical, commercial, or societal nature. As a result, new products require exhaustive testing over long periods of time before they can be brought to the market.

Clearly, biotechnology can be a high risk, high reward business area.

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Opportunities for Innovation in Biotechnology Health Care

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The environment for delivery of health care is changing worldwide and its place in the socio-economic hierarchy is undergoing a great deal of scrutiny by payers, providers, policy makers and patients. The definition of quality health care more and more is becoming a question of balance between cost of care and measurable (economic) patient benefits. This dichotomy and its impact on health care policy development has been fueled significantly by the phenomenal technological advancements which continue to be made in medical diagnosis and therapy. In addition, the future promises that new therapies and diagnostic methods can be developed to cure or significantly ameliorate many diseases which are presently unapproachable. Biotechnology will be one of the fundamental tools used to address these problems. However, the commercial development of health care products derived from applied biotechnology must be made with a thorough awareness of the risks and constraints which are inherent to the field and developing in the world. The new health care environment will not accept developments made for the sake of technology alone. They must be tied to measurable health care benefits which are the result of positive patient outcomes in comparison to alternative means of patient management.

This article is intended to summarize broad issues in the commercialization of biotechnology-based products directed toward the health care sector. Hopefully, it will provide an initial resource by which to measure the likelihood of commercial success of a given biotechnology opportunity. It is not intended to be a comprehensive assessment of potential opportunities which exist or which can be met by biotechnology products.

Key words: cost-containment; diagnostics; pharmaceuticals; therapeutics.

1. Market Drivers In Health Care Innovation

1.1 Unmet Medical Needs

First and foremost, the opportunity for any therapeutic (in this paper, the term therapeutic includes vaccines) or diagnostic product will be defined against the needs which exist, the degree to which they are currently satisfied (or unsatisfied), the size of the target population and the frequency with which the "product" will be used. This defines the "market." Examples are provided in figure 1, which charts the treatable patient population for a set of diseases against the degree to which the need remains unmet. Such graphic illustrations are useful to obtain a relative gauge on commercial potential should the product concept be technically successful. The role of biotechnology at this level is only as one of a number of potential approaches or as a tool by which to meet the need by developing the product. The technology is the process, not the product.

Multiple factors are included in defining and quantifying unmet medical needs and then relating a proposed technological advancement to its role in the market. The size of the patient population to which the therapy will be directed is a primary consideration. These numbers can be obtained

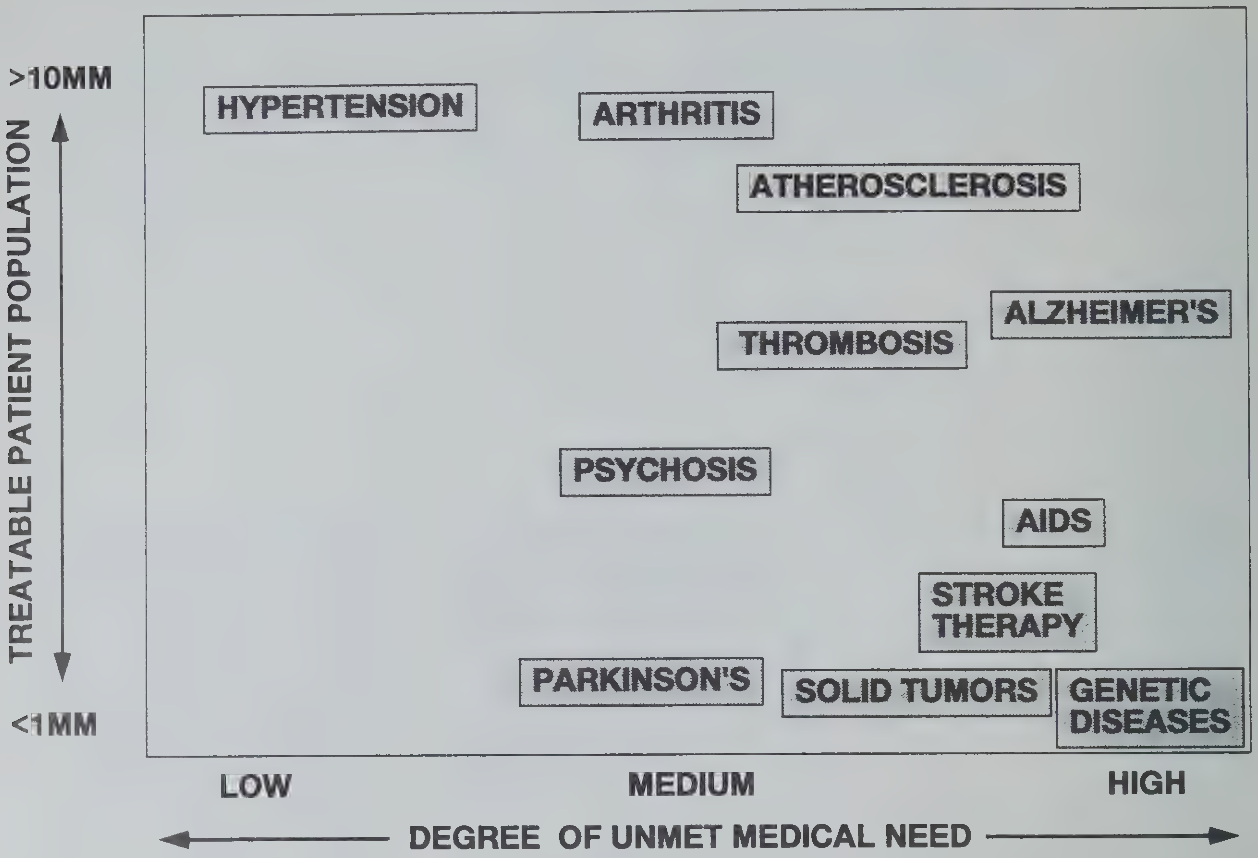

Figure 1. The relationship between the size of the treatable patient population and the of degree satisfaction of medical needs with current therapies. The treatable patient population (y-axis) represents the number of patients in Europe and North America who have the indicated disease and are available for pharmacological therapy. These estimates are based on published epidemiological data obtained from a variety of sources combined with drug marketing data of penetration rates into the specific disease population. In general, there is an inverse relationship between the size of the patient population for a given disease and the degree to which the medical need is satisfied. The genetic disease pool represents a composite of documented genetic disorders and does not include diseases in which a genetic component has been implicated.

from actuaries, medical societies, government databases and the medical literature. In addition, the epidemiology of the disease or diseases targeted should be well understood: is the disease stable in the population (e.g., multiple sclerosis), is it increasing in some selective group (e.g., Alzheimer's disease in the aged) or is it epidemic (e.g., AIDS)? Are there core technologies which will be applicable to a number of diseases and which, with generic modification, will expand the basic application?

Next, the size of the opportunity needs to be assessed in perspective of the degree to which it is already treated or is likely to be treated at the time the novel therapeutic development is introduced. If the drug should be directed at specific subsets of the overall patient population, these need to be defined. For example if some patients are resistant or refractory to an existing regimen, or if the therapeutic concept is likely to be useful only at a specific stage of disease, the applicable patient populations will be limited and the product applications will be more narrowly focused. For diagnostic applications, a key consideration for ultimate acceptability and use will be the impact a diagnosis has on therapeutic decision making. Diagnosis and therapy are inexorably linked, yet the cost pressures and controls on diagnostics are likely to be even greater than on therapeutics.

Therapeutic medical needs may not always be defined by a specific disease. Some of the biggest success in biotechnology to date have been adjunctive therapies for amelioration of treatment-related problems. Amgen currently is viewed as the "flagship" biotechnology company based on 1991 sales of $409 million for Epogen (erythropoetin) replacement therapy in kidney dialysis patients and $233 million in sales for Neupogen (recombinant granulocyte-colony stimulating factor, G-CSF) which stimulates white blood cell production in cancer chemotherapy patients. These products fulfill major unmet needs in creative market niches that are not related directly to the etiology of a disease.

The degree to which current therapies (and diagnostic methods) satisfy medical needs will be a key factor in the success of future technology applications. The replacement of effective therapies by "me-too" versions, differentiated only on the basis of the technology source, are not likely to realize long-term success in the future environment of cost-containment.

1.2 Trends in Cost-Containment

The medical credo for the nineteen nineties is "give value for money." It is almost a given, and proven by precedent, that novel therapies based on biotechnology will be relatively expensive. Biotechnology companies that have been "successful" have invested heavily in risk and promise. In addition, production costs of biotechnology (e.g., recombinant) products, in general, are high relative to their pharmaceutical counterparts. An example of a confounding future cost issue is that some therapies (e.g., gene therapies) offer the promise of being curative following a single administration. It may be very difficult to obtain a price adequate to achieve an acceptable return on a therapy which is given infrequently to a small population.

The financial and product status of a cross-section of major U.S. biotechnology firms is shown in Table 1. This table illustrates that the productivity of the biotechnology industry in health care has been quite low, and that most companies have few products to show for their efforts. The time between inception and commercialization of therapeutic biotechnology products in the United States averages 6 years for those that have "made it." Those that have yet to "make it" average 9 years in trying.

As major advances in biotechnology improve the means to discover and develop novel therapies, governments and third-party payers will increasingly scrutinize health care costs and develop means for their containment. Recent landmark developments in the introduction of biotechnology products highlight the issues which future manufacturers must face. In a recent overview, Campbell, et al., [3] admonish those considering entry into biotechnology ventures to gain a firm appreciation for reimbursement and pricing issues. Third party payers and providers increasingly are scrutinizing the horizon for means to reduce their out-of pocket expenses. High-priced biotechnology products are obvious and easy targets for noncoverage. Indeed, much of this current scrutiny has been brought on by the biotechnology industry itself.

Cost-containment and health care resource allocations are international issues. For example, France recently adopted a set of guidelines on which to base reimbursement levels for new products as a function of the benefit it brings to the patient [4]. Products are ranked into one of six benefit categories, ranging from a major therapeutic advancement to offering benefit but no improvement over current therapies to unfavorable, by the French Transparency Commission. These ratings translate to the level of pricing reimbursement which the government will sustain. Clearly, it is becoming more and more incumbent

Table 1. Financial and product profiles of selected major U.S. biotechnology companies[a]

Company	Capitalization ($million)	1991 Sales ($million)	1991 Earnings per Share	Proprietary Marketed Therapeutics	Year Established	Year of First Product Launch in US
Amgen	$8,131	$682	$0.67	2	1980	1989
Genentech	$3,233	$515	$0.39	3	1976	1982
Chiron	$1,660	$118	($22.11)	2	1981	1987
Synergen	$1,170	$0	($0.36)	0	1981	N/A
Gensia	$1,078	$3	($1.25)	0	1986	N/A
Genzyme	$1,071	$81	$0.71	1	1981	1991
Biogen	$795	$70	$0.15	1	1978	1986
Genetics Institute	$706	$82	($1.05)	1	1980	N/A
Immunex	$465	$63	$0.05	1	1981	1991
Centocor	$463	$44	($3.67)	1	1979	N/A
US Bioscience	$452	$3	($0.18)	1	1987	N/A
Immune Response	$347	$0	($0.23)	0	1986	N/A
Cytogen	$336	$0	($0.98)	0	1980	N/A
Liposome	$258	$0	($0.22)	0	1981	N/A
Medimmune	$249	$6	$0.11	1	1988	1991
Immunomedics	$239	$1	($0.20)	0	1982	N/A
ICOS	$186	$0	($0.31)	0	1989	N/A
ISIS	$125	$6	($0.84)	0	1989	N/A
Sphinx	$96	$0	($1.19)	0	1987	N/A
Agouron	$84	$0	($1.42)	0	1984	N/A

[a] Modified from [1] with input from [2].

upon manufacturers to demonstrate that their "innovations" are measurable advancements in terms of both clinical and economic outcomes.

Genentech is considered one of the star examples of a successful biotechnology company, and was the first to make it to market with what was purported to be a major therapeutic breakthrough. The product, tPA (tissue plasminogen activator, Activase) is a recombinantly-produced homologue of a naturally occurring human enzyme for clot lysis, the treatment of acute myocardial infarction. The product was approved by the FDA in 1987 and introduced at a price approximately ten times higher than the generic competitor, streptokinase, a bacterial enzyme. Perceptual expectations were raised within the cardiology community that tPA should be a better thrombolytic than currently available agents. However, endpoints by which "better efficacy" was defined were clouded. In the flurry of excitement over the introduction of a new technology, tPA was adopted rapidly by providers. In the United States, this had a clear and immediate impact on the reimbursement schedules for the management of acute myocardial infarction. In fact, in controlled clinical trials which were published after its market introduction, Activase has been shown to offer no measurable clinical advantages over streptokinase, leaving the provider with few means to justify its use at the current cost [5]. While annual sales of tPA reached over $200 million, this is far short of the $800 million–$1 billion which were projected prior to its approval. The sales of tPA peaked only 2 years after launch and its share of the thrombolytic market now is declining.

Centocor offers another example of the pitfalls that can occur when innovative, but poorly-focused products are developed. Centocor concentrated its efforts on the use of monoclonal antibodies for *in vivo* diagnosis and therapy. Its first product was Myoscint, a radio-labeled monoclonal antibody against myosin, to diagnose acute myocardial infarction. The project demonstrated to the financial community (and to Centocor) that Centocor could develop, manufacture and register an antibody-based product. However, the medical need to diagnose an acute myocardial infarction 24 hours after the event is minimal and the technology is difficult to justify on a cost basis. The product has yet to be approved in the United States and likely will find a very small niche in transplant rejection and diagnosis of cardiomyopathies; far different than the larger, targeted indication.

While Myoscint never was predicted to be a major drug, the expectations of Centoxin were much higher. Centoxin, a human monoclonal antibody (MAb) against bacterial endotoxin lipid A, is proposed to be indicated for the treatment of shock associated with gram-negative bacterial sepsis. While there is a major unmet need to treat sepsis and associated shock, appropriate patients (i.e., those that have gram-negative sepsis) are difficult to identify prospectively. Since only 30% of septic shock patients have gram-negative bacteremia and the drug is estimated to cost nearly $4,000/dose, a great deal of concern is being raised among providers and payers on its appropriate application. Moreover, Centocor inadvertently raised the cost-benefit question at the FDA when the product was introduced in the Netherlands at $3700/dose during the FDA review process. As Centoxin moves closer to approval in the United States it faces two major hurdles to its success: 1) Increased price scrutiny by third-party payers and providers and 2) the advent of more effective, better targeted therapies.

A more immediate and publicly visible cost-benefit issue has be brought to the forefront by the recent introduction of Ceredase (placenta-derived alglucerase), by Genzyme. Ceredase is an enzyme replacement therapy to treat Gaucher's disease, a genetic abnormality in which the lack of the enzyme results in abnormal lipid accumulation in macrophages. Since therapy with the drug can cost up to $750,000 per year [6] its use is being debated hotly even at the Congressional level. While it is estimated that Genzyme will reap sales of approximately $95 million in 1993 on Ceredase [7], it is likely that the company will be under substantial scrutiny and criticism to justify these enormous per patient costs. Fortunately this cost issue may be resolved to some degree as Genzyme is planning to submit a marketing application for recombinant Ceredase, which might reduce manufacturing costs somewhat.

These examples reinforce that biotechnology only is a potential means to an end. Biotechnology products (and companies) will succeed if they bring unique and measurable benefits to the patient and reduced cost to society. Ultimately, however, they will compete in the market under traditional circumstances and will not be valued based on technical novelty.

Current trends in health care cost-containment already are having a major impact on the way biotechnology products are and will be used throughout the world. Because of the uniqueness, promise and visibility of biotechnology products, they will continue to be exemplified as the future of health care as well as a primary source of innovative advancement.

2. Technology Assessment: Idealizing Risk and Reward

2.1 Proof of Concept:

The first question that must be addressed to measure the likelihood of commercial success is: How likely is it that the technology can be reduced to practice? The likelihood of positive proof-of-concept is a continuum in which probability is increased as knowledge is gained or milestones are met. Most of the successful biotechnology companies to date have obviated this risk by starting high in the continuum. In the development of their early products, Genetech and Amgen, for example, were dealing fundamentally with manufacturing issues. There was no quibble about the likelihood that tPA could dissolve a clot, that human growth hormone or insulin would be efficacious or that erythropoetin would stimulate red blood cell production in anemic states. The big hurdle, proof of efficacy in man, was a given with these products. For most potential products, assessment starts much earlier in the proof-of-concept continuum and the questions which need to be addressed hierarchically include:

- Does the target system produce a pharmacological or physiological effect if perturbed?
- Can a drug be designed rationally to evoke this response?
- Can the drug interaction be represented in an in vitro system?
- Can the drug interaction be reproduced in an animal model of efficacy?
- Can efficacy be demonstrated in nonzhuman primates?
- Is there a clearly defined mechanism of action?
- Is there an available assay of pharmacodynamic efficacy in man?
- Is there a surrogate marker for efficacy in man?
- Can pharmacological effect be demonstrated in man with and without surrogate markers?

As each of these milestones is addressed, the probability of positive proof of concept is increased. As will be shown, proof-of-concept is only one factor in determining the likelihood of technical success. A determination of the probability of ultimate marketing success of the product should be considered in terms of other technical hurdles such as safety, ability to formulate, manufacture and deliver, as well as any regulatory issues which may face its review and approval.

2.2 Competitive Position:

Many technologically based enterprises are expert in assessing proof-of-concept for a given area of innovation. After all, the concept usually is the basis of formation of the company. Often however, this is where technology assessment ends with start-up firms eager for investment dollars. As exemplified above, successful health care innovations are unlikely without a clear understanding of the competitive environment in which they exist. Any product or product-oriented project must be assessed continually against current and future competitive pressures. Early products only can be evaluated conceptually, but this must be done with brutal objectivity under a range of profile conditions.

A thorough understanding of the current and dynamic nature of the competitive environment is essential to long-term success. Health care innovations are subject to the same general competitive pressures as any other industries [8]. Thorough awareness of the current competitors, the threat of new market entrants, the threat of substitute products and the bargaining powers of both suppliers and potential buyers cannot be overlooked. In general, biotechnology firms will be operating under a competitive strategy of product differentiation, not from a cost-leadership position. Again, differentiation ultimately will be defined by the relative health outcome benefits of the product, not by the technology alone.

2.2.1 Timing. Timing, of course, is a key component of competitive position. In the broad sense, the concept of timing relates to the relative advantages biotechnology may bring to the drug development and discovery process. Biotechnology, is by-definition, rational. The identification of drug targets and the conceptualization and design of molecules to accomplish specific molecular interactions is a competitive strength of biotechnology. A recent report [9] shows a mean time of over 12 years from synthesis to marketing approval of a new drug, and 9 years to approval once a drug has entered clinical trials. These estimates do not include the time required to identify the preferred chemical structure for drug development. A retrospective study by Bientz-Tadmor, et al., [10] demonstrates that in general, and especially for recombinant DNA products, the duration of clinical development is shorter and clinical success rates are higher than with standard pharmaceuticals (new molecular entities). However, these improved success rates and statistics are somewhat skewed and optimistic since they are based on molecules formed from human genetic constructs (i.e., endogenous molecules) with reasonably well-defined activities and toxicities. As exemplified earlier, the trial and approval process for monoclonal antibody products has proceeded as smoothly as the recombinant molecules.

As technology expands into the discovery and development of modified bio-molecules, technical success rates and clinical development timelines likely will normalize with conventional pharmaceuticals. For example, anti-sense DNA or RNA constructs are being investigated as means to modulate genetic expression. A major focus in the development of anti-sense molecules as drugs relies on back-bone modification of the order to idealize activity in vivo. Even more radical modifications, such as novel base derivatization, are being pursued. These molecules, based on natural sequences, but chemically and biochemically novel, will be new molecular entities and will be treated as such in development and registration.

In a narrower sense, timing, like R&D and capital cost, is an element of corporate exposure. Realistic estimates of the time required to reach each key decision point in a project need to be made. Estimates of time should be made in reference to standard industry benchmarks. For example, the average time between submission and approval of new molecular entity by the FDA is about 30 months. Shorter estimates based on the technology may sell well on Wall Street, but ultimately will lead to investor frustration and a misrepresentation of value by the firm.

2.2.2 Durability. The durability of any technology (especially in health care) relates to its protection under patent laws or extension of exclusivity by other means. The patentability of biotechnology products continues to be one of the major issues facing the industry. Concepts of patent law are being challenged from multiple directions. The U.S. Patent and Trademark Office to date has rejected patent applications on human gene sequences which NIH has filed on work emanating from the human genome project. Key questions remain about novelty and obviousness of a gene sequence which has no identified function. Deeper questions remain about ownership of what is constitutive in humans already. The international patent issues surrounding tPA and other recombinant products which are constitutive in humans, suggest that the concepts of novelty do not have universal definitions. The Genentech patents claims which were allowed in the United States, after 6 years of review, were found to be invalid in Great Britain due to lack of inventiveness. The patents claims which were allowed in the United States issued one to two years after the product was commercialized, a very tenuous and high risk position for Genentech and its investors.

Biotechnology firms will continue to form and attract investors based on patent applications, not on issued claims. Given the unpredictability of patent outcomes and the time required to obtain them, this is a risk inherent to timely commercialization of new technology. Clearly, in the pharmaceutical industry, composition-of-matter claims based on novel chemical structures provide the strongest competitive position.

Protection of some technologies can be realized under the Orphan Drug Act, which provides a 7 year extension of exclusivity for products which are developed for small markets (under 200,000 patients per year in the United States). It should be recognized that this law does not relax requirements to prove safety and efficacy prior to marketing. However, since patient numbers for orphan indications are relatively small and the needs high, the FDA might relax patient numbers normally required and the rules to provide two, adequate, well-controlled clinical studies for registration. The trade-off would be a commitment to continue firm-sponsored post-marketing studies as well as extensive post-approval safety surveillance. In addition, rules are being considered to limit exclusivity under the act to those drugs which have annual sales volumes under a specified threshold ($200 million has been proposed). Chew [11] provides a review of the implications of the Orphan Drug Act.

2.2.3 Barriers to entry. Porter [12] deals with the unique competitive issues related to market entry in an emerging industry like biotechnology. These barriers include the proprietary technology itself, corporate access to capital and human resources, raw material supply, supply of enabling technologies, and the opportunity cost of capital. A barrier with some uniqueness to the health care field is the learning curve to ensure acceptance of novel technologies applied to humans. While, as in the case of tPA, new technology can be embraced quickly, more radical therapies will require significant patient, payer and provider education to gain acceptance. Products which alter human phenotypes and genotypes likely will be accepted slowly as the roles for such therapies become defined experientially.

2.2.4 Costs. Like timing, cost estimates to the completion of the project or to the realization of key milestones need to be made realistically using industry averages as a base case. Current industry average costs to fully develop a new therapeutic are $200-250 million, including failed project costs and cost of capital [9]. A breakdown of industry average R&D costs by stage of development is provided in Table 2. The costs of development could be much lower if the company bets right the first time (i.e., has no failures in the development phase) but on an individual basis a new molecular entity still will require an investment of $70-90 million in real dollars through approval.

Table 2. Average allocated costs by stage of development for a new molecular entity, therapeutic drug[a]

Development Stage	Allocation (%)	Cost ($ Million)
Discovery	23%	$53
Pre-Clinical	15%	$35
Phase I Clinical	21%	$48
Phase II Clinical	23%	$52
Phase III Clinical	15%	$35
Regulatory	3%	$7

[a] Modified from [13]

2.2.5 Regulatory Hurdles. The regulatory hurdles to the marketig approval of new therapeutic technologies have already been alluded to in other sections. The regulatory environment is consolidating so that technical approvals are becoming more closely affiliated with pricing and cost-benefit issues in the world's health care regulatory agencies around the world. Regulatory issues will be unique to a given technology and to a given product application. Even though the FDA has implemented tactics in the Center for Biologics to streamline the review process, regulatory agencies will not deviate from requiring scientifically and statistically sound applications in order to approve a product for marketing. For promising products that truly meet needs which are poorly addressed, agencies are likely to give priority reviews and the process could be accelerated, but this is likely to be the exception.

3. Technology Transfer: Innovation to Commercialization

3.1 Strategic Considerations

Experience in the high-risk, issue laden development of the biotechnology industry has led to a major shift in emphasis toward realizing commercial success. Historically, in the infancy of a firm, success has been defined as the use of the technological base to build a framework of commercial opportunity and then to build a fully integrated, global company based on the technical innovation. The lessons of the last 15 years have taught that, while this may remain a vision, it probably is an unrealistic goal. The pitfalls to the application and development of a single technology in the health care arena are innumerable and mostly unforeseen. As will be evidenced, the most successful biotechnology companies to date have begun to build their financial base more broadly than on investor funding and public offerings. They have begun to implement strategies for more rapid commercialization of near-term products (not necessarily "high-tech") to support corporate growth and to provide internal funds for R&D on the proprietary technology which forms the base of the company. These strategies include acquiring near-term or marketed product rights, penetrating foreign markets, streamlining development of technological advances and gaining access to broader market segments to increase the likelihood of becoming a fully integrated pharmaceutical company. This way, the company can demonstrate a path to solvency and be prepared for ultimate commercialization of the founding technology.

Although development and commercialization of a single technology or product can be a successful strategy (e.g., Amgen), this is not the rule. Capital investments that are able to stay with a company through the eight to ten years required for commercialization (once the product candidate is identified!) are becoming more difficult to sustain. Also, given the vagaries of the regulatory environment and unpredictability of clinical trial outcomes, reliance on a single technology can be devastating if it fails. Centocor based its success on the use of monoclonal antibodies in diagnosis and therapy, and built manufacturing and sales capabilities in advance of product approvals. They now have two products pending at the FDA, both with modest efficacy or for use to address minor unmet medical needs. Even though they had 1991 revenues of about $44 million, this is inadequate to sustain a sales force of 200, which they built in anticipation of new product approvals. The go-it-alone strategy is unlikely to pay-off for Centocor.

In order to militate against similar situations, companies are beginning to ply their technology earlier in hopes of building positive cash flows sooner in the commercialization of technology. As the availability of public capital decreases, companies see strategic alliances with larger, more diversified companies as one attractive alternative. A strategic alliance can be beneficial in that it provides credibility to the technology and can foster further investment. In addition, it may provide access to larger and more experienced development capabilities and thus accelerate the development of the product. The downside is that an alliance on the technology "trades-off" the foundation on which the company is based and can be a very expensive deal in the long run. Additionally, a strategic alliance with the wrong partner can result in delay of commercialization if the licensed technology falls prey to shifting priorities and resources in a larger corporation. It is difficult to assess the global value or success of the various alliances that have been made, since overall, marketed products have yet to be born from them. While the number of alliances based on therapeutic biotechnology products remains intense (109 alliances formed in 1992) the intensity may be declining from previous years [14]. Moreover, the nature of these alliances appears to be shifting from vertical alliances with major pharmaceutical companies to lateral alliances among biotechnology companies [15].

Increasingly, companies are building and diversifying by gaining access to product lines which may not be "biotechnology," but meet short-term goals of commercialization. Athena Neuroscience, devoted to the amelioration of major diseases of the central nervous system (CNS), swapped one of its long-term technologies for a near-term product from American Home Products. Also, it has acquired a line of branded generic CNS drugs for home delivery. They are using this business to build a sales force, gain access to a target market audience for future proprietary products and maintain credibility with investors through generation of revenues.

The road to commercialization of a given technology in the human health care arena is arduous and risky. Start-up biotechnology companies are identifying and implementing strategies to allay risk earlier in the development phase of proprietary technology and to ensure that the technological basis of the company eventually can be realized through commercialization.

3.2 Issues, Opportunities and Rewards

While fraught with cautions and admonitions and a history laden with far more failures than successes, biotechnology remains the key to the future development of efficacious and cost-effective therapeutics and diagnostics. In 1990, the worldwide sales of health-care related bio-pharmaceutics and diagnostics totaled approximately $3 billion which supported a research and development expense of similar magnitude. In comparison, worldwide sales of ethical pharmaceuticals totaled nearly $200 billion with $12 billion in R&D expenses [15]. By 2000, the total sales of biotechnology products for health care applications are expected to reach over $30B. While the growth in the introduction and sales volumes of biotechnology-based products for health care applications has been explosive, the industry remains heavily invested and, as a whole, unprofitable [1].

3.2.1 Delivery Systems. The current pattern of use of biotechnology products in health care (both diagnostic and therapeutic) is on an acute or intermittent basis given via a parenteral (i.e., "invasive") route. Systemic delivery options for large biomolecules currently are limited and delivery technology is in its infancy. Almost all marketed drugs in use today are small molecules delivered orally. The inability of biotechnology products to follow patterns of standard therapy has been a major limitation to the expansion of the industry [16]. The human body has formidable physical, chemical and biochemical defenses against the introduction of foreign carbohydrates, polypeptides, lipids and nucleic acids at the corporeal, organ and cellular levels. Means to circumvent these defenses in order to deliver constitutive biochemical or novel macromolecules by less invasive means are being developed, but are in their infancy. Core technologies to deliver genes non-invasively in a controlled, "reversible" and intermittent way are being investigated using viral vectors for example, or altered cell-types. Means to deliver macromolecules through the skin or mucosa could provide integral leaps in the use of biotechnology drugs and would be highly marketable enabling technology. In addition, organ specific delivery or targeting systems, such as means to carry drugs or macromolecules across the blood-brain barrier could radically improve the treatment of diseases of the central nervous system. Also, better means to deliver macromolecules, such as anti-sense oligonucleotides, across the plasma membrane into cells need to be developed in order to obtain maximum utility from cellularly targeted therapies. Major commercial opportunities exist if any of these delivery barriers can be overcome with practical technology.

3.2.2 Drug Discovery. A major and growing application for biotechnology is as an enablement to rational drug discovery and design. However, the financial opportunities in discovery services are not likely to be large. Most major pharmaceutical companies have either internally directed programs or access to enabling technologies through alliances. Discovery groups routinely are using biotechnology to clone and express receptors in cultured cells for chemical screening. Also, interactions of natural ligands with their receptors can be studied and modeled as a means to direct chemical synthesis of enzymatic inhibitors or receptor agonists and antagonists. The ultimate purpose of these efforts usually is to design a small heterocyclic molecule (not a bio-pharmaceutical) which can be developed into a "standard" drug. Another enabling role for biotechnology is the production of specific animal models of diseases unique to humans. The use of transgenic animals in cancer research and drug discovery is well-established. A recent failure of these animal models was the inability of transgenic rats to express meaningfully the genes associated with familial Alzheimer's disease [17]. While some companies have been set up on the basis of providing research tools for discovery (e.g., Nova, Affymax, Agouron), these companies generally intend to find a proprietary agent using their core technology, not only to perform service for hire.

3.2.3 Diagnostics. Diagnostic products that have been enabled by biotechnology or are of biological origin have been and will continue to be a mainstay of the health care industry. The worldwide sales of all diagnostics was over $21 billion in 1990, with a 66/33 split between in vitro and in vivo (imaging) products. This represents an increase of 11% over the previous year [18]. An additional $23 billion in revenue from clinical testing services was realized in 1990 in the United States alone. Major niche opportunities for in vivo and in vitro diagnostics remain open for development.

Areas of need for in vivo diagnostics generally implies the use of medical imaging. The technologies which support imaging are based in linking a molecular or atomic characteristic for detection (e.g., paramagnetic, radioactive, ultrasound or electron density) to a targeting molecule (e.g., metabolically active, antigen specific, DNA-sequence specific) to obtain functional imaging of disease. Needs exist to differentially diagnose neurological disorders (especially dementia's) as new therapies develop for these diseases are developed and applied. In vivo opportunities in cancer diagnosis include the differential diagnosis of malignant from benign lesions to reduce biopsy rates and to monitor the course of cancer therapy. In addition, needs exist for the non-invasive assessment of fevers of unknown origin in AIDS, surgery and trauma patients. Products to meet these needs could provide $300-$500 million in additional revenues.

The already dominant position of biotechnology in in vitro diagnosis will continue to grow stronger. The diagnostic industry is consolidating and clinical laboratory procedures are moving from office-based to managed care environments. This will set the stage for the introduction and routine use of more sophisticated and technically demanding methods. Current trends include meeting the need to increase sensitivity and specificity of immunoassays and cell cultures by using DNA probe technology. Also, the development of biosensors to monitor therapeutic drug levels, for drug and alcohol abuse or monitoring of cholesterol and other metabolic endpoints is proceeding rapidly. The increase in AIDS has opened the door for more specific assays to identify HIV strains, monitor viral burden, follow development of drug resistance and provide more accurate prognosis in treatment populations. While regulatory approval and market introduction intervals from discovery are substantially shorter compared to in vivo products, the product life cycles also are shorter for in vitro diagnostics.

4. Summary and Conclusions:

The purpose of this paper has been to provide a paradigm for identification and evaluation of opportunities which exist to use biotechnology tools to discover and develop new products for human health. The nature of health care delivery is changing rapidly worldwide, and new applied technologies are under increasing pressure to prove "cost-effectiveness" in order to be accepted into medical practice. Entry into technology-based ventures should be undertaken with due consideration of the risks associated with any new therapeutic or diagnostic method. A thorough understanding of unmet medical needs which the product or product concept could address, the competitiveness of the product and markets and health care delivery systems into which it will be introduced will provide a real competitive advantage to biotechnology-based companies. Biotechnology holds the promise to improve the diagnosis, treatment and cure rates for many diseases which so far have remained elusive to standard drug technology. While a superficial analysis of the value of health care products based on biotechnology may argue in favor of their broad application, society increasingly is concerned with cost as a primary component of acceptability. Successful biotechnology entrepreneurs must develop and maintain a keen sense for the economic ramifications of their science.

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Opportunities for Innovation in Biotechnology Crop Agriculture and Forestry

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1. Introduction and Overview

Traditional crop agriculture made incredible advances in productivity as yields increased over 300% during the last half of the 20th century. This resulted from the incorporation of new mechanical and chemical technologies for the control of insects, diseases, and weeds. Traditional plant breeding was another technology which played a significant role in this advance. Hybrid corn, the most profitable segment of the commercial agronomic crop seed business, was an example of the contributions made by traditional plant breeding as it made continuous year-to-year improvements in yields following its introduction toward the middle of the 20th Century.

Other contributions of the traditional plant breeders included the nectarine (a genetically modified peach) and the tangelos (a hybrid of the tangerine and the grapefruit). These novel foods added diversity to the food supply.

Basic discoveries concerning the structure of DNA in the 1950's and 1960's coupled with new capabilities to cut and splice portions of this genetic code in the 1970's, has given rise to modern biotechnology and the promise of remarkable opportunities for the future based on the application of this technology.

Modern biotechnology as used in this discussion can be broadly defined as the utilization of biologically derived molecules, structures, cells or organisms to carry out specific processes to improve plants or develop microorganisms for specific uses. The two dominate characteristics of this technology are its precision and the power to cross boundaries not possible to cross through traditional plant breeding.

Biotechnology has the inherent potential to enhance the production, processing and marketing components of crop agriculture to a level far exceeding that brought about by the mechanical and chemical technologies of the 20th Century. Plants produced utilizing the techniques of modern biotechnology such as recombinant DNA, i.e., transgenic plants, are expected to have commercial potential by meeting grower and consumer needs for improved productivity, improved value-in-use, expanded non-food and non-feed uses and environmentally neutral crop production practices.

The potential for products derived from biotechnology are immense if one simply considers the projected growth of the world's population from the current level of approximately 5.5 billion to an estimated 10 billion people by the year 2040. This represents essentially a doubling of the population while the land available for crop production dwindles rapidly as a consequence of the twin forces of urbanization and the competing concerns for the non-agricultural use of the land for wetlands and the preservation of wildlife [1].

The challenges to enhance the productivity of agriculture, generally referred to as "production agriculture," extend beyond the normal technical arena as there is little doubt the commercialization of products derived from modern biotechnology will be viewed with intense scrutiny by the general public. Much of this results from the uncertainty the general public has concerning genetic engineering and their perception of the risks associated with genetically modified foods. The willingness of the public to accept the products of modern biotechnology is the critical factor in determining how successful this technology will become.

The impact of biotechnology on crop agriculture will occur in several ways. Crop productivity especially for commodities will be improved, international competitiveness will be intensified, foods and feeds with increased value-in-use will enable increased profitability with their identity preserved rather than as commodities, the percent of discretionary income spent on food will increase, nontraditional uses of plants will explode in the longer term to become a major highly profitable market for plants that directly produce high performance polymers and the relationship between crop production and the environment will become more friendly.

These changes will undoubtedly create opportunities for new businesses and realignment of traditional businesses will certainly occur. This will impact the agribusiness input industries such as fertilizers, agrichemicals, and seeds in response to the maturation of the fertilizer and agrichemical industries and to the expected commercial opportunities and impact of transgenic plants. The major commercial opportunity for transgenic plants is expected to be the production and sale of seeds. Chemical and pharmaceutical companies are acquiring seed companies; others are establishing relationships with seed companies and/or food/feed processing and distribution companies. A small group of development-stage biotechnology companies with leading technical capabilities are focused on transgenic plants and their commercial application; several established agrichemical, pharmaceutical, and seed companies are also emphasizing transgenic plants and their commercial opportunities.

The discoveries for the first generation products in agricultural biotechnology occurred within the last decade (Table 3), thus the lead time from discovery has been relatively short. However, it should be emphasized that no genetically modified foods have yet gained regulatory approval for commercial sale. Calgene, the developers of the Flavr Savr ™ tomato, have submitted a request for an advisory opinion from FDA and expect a favorable response before the end of the year with sales of seed to begin shortly afterward. The regulatory guideposts for biotechnology are yet to be unraveled and will be critical factors in determining the length of time and the costs of reaching the marketplace.

With such projected needs in terms of the food supply and the role for products derived from biotechnology and the vast potential for new products it is not surprising that major companies either have or are currently spending considerable sums of money on R and D to discover and commercialize products for this market place. However, one of the important aspects of biotechnology is that it does not require intensive capitalization to develop products and it also offers major opportunities to penetrate so-called niche markets—markets that organizations with substantial overheads can not afford to consider. Consequently, there are many opportunities for small to medium sized businesses to gain access to the potential markets.

In this chapter, we shall examine the opportunities for crop agriculture and forestry, the technical status that underpins those opportunities and evaluate the constraints that must be overcome to reach the marketplace.

Table 3. Recent advances in plant biotechnology

1st expression of a plant gene in a plant of a different species	1983
1st EUP from EPA for release of GMO (P. syringe and P. fluvesences) in which the gene for ice-nucleation protein has been deleted	1985
1st patent for sexually reproduced plants (corn)	1986
1st approved field test-stopped at vegetative stage	1986
1st genome sequence-tobacco chloroplasts	1986
Introduction of luciferace gene into plants	1987
Regeneration of single cells-rice	1987
Introduction of foreign genes into cereals	1987
Extended shelf-life using "antisene RNA" (tomatoes)	1987
1st approved field test of a genetically engineered biopesticide (Mycogen)	1990
1st EPA approved genetically engineered biopesticide for sale in the USA	1991

2. Potential Impacts of Production Agriculture Including Forestry and Food/Feed

Biotechnology is expected to have major beneficial economic, environmental, and health impacts on agriculture and food. These new products will include substitutes or complements for existing products of seeds, microbes, animals, agrichemicals, fertilizers, etc., as well as products for unmet needs and will have major market impact.

2.1 Agribusiness Impacts

2.1.1 Seeds—The major impact of biotechnology will be on the seeds component of the agribusiness industry as seeds or the equivalent genetic material for vegetatively propagating plants are the primary inputs for crop production. The annual value of world seed use is about $50 billion, including $15 billion of commercial seed sales in 1988 [2]. Revenues [3] for the leading seed producers is shown in Table 4. Transgenic plants are expected to increase the world seed use value to about $100–$150 billion early in the 21st century with the increases coming from values created by improved productivity, improved value-in-use and expanded non-food/non-feed uses.

The value of transgenic plants has caused many commercial companies to visualize the seed business as a major growth opportunity. This is illus-

Table 4. Ranking of seed companies (revenues)

Company	Revenue ($ millions)
Pioneer Hi-Bred International, U.S.	788
Sandoz, Switzerland	488
Group Limagrain	360
Upjohn (Asgrow)	256
ICI Seeds	238
Cargill	236
Ciba	197
Dekalb	190
Sica France Mais	170
Takii &Co.	170
KWSAG	160
Ste. L. Clause	159
Sakata	152
Cebeco	146
Weibull	123
Unilever	110
Sanofi	107

trated by the number of seed companies that have been acquired by established or development-stage companies with existing strong technology in transgenic plants as well as by some established companies seeking to acquire this technology for transgenic plants (Table 5). These strong technology companies recognize that they need established seed companies to provide quality germ plasm for production of transgenic plants as well as to provide a route to market their transgenic plant technology as seeds.

Table 5. Comparisons of positions of Japan, Europe, and the United States on various technologies that support crop agriculture

	JAPAN			EUROPE		
TECHNOLOGY	Lag	Parity	Lead	Lag	Parity	Lead
Plant transformation	S			→		
Plant cell culture	*		*			
Selectable markers		*	*			
Gene regulation	*	*				
Gene mapping	*	*				
Gene sources	S		*			
Forest technology	*(?)	*				

* The chart is intended to provide a visual comparison of where Japan and Europe stand in comparison to the United States. The symbol "*" is used to indicate a relatively stable position. An "S" indicates a substantial lag or lead and the → arrow indicates that the country is gaining on the United States and the ← arrow indicates the United States is gaining on the country.

Currently, only about 20% of all planted seed is purchased with 80% being seed grown by the farmer and saved from his previous crop (plant-back seed). The rates of purchased to plant-back seed ranges from over 90% for hybrid corn to almost 0% for some specialty crops such as radishes. While factors such as improved genetic value of the purchased over plant-back seed, the proprietariness of the purchased seed, and the increased size and management of crop farms will favor purchased rather than plant-back seed, the grower places a premium on increased yields. Thus high-yielding germplasm is essential for the use of purchased seed for commodities such as soybeans, wheat, cotton, sorghum, etc. to increase.

Among existing seed companies, Pioneer Hi-Bred International is the largest. With $1.26 billion in total annual sales in 1992 over half of which came from corn, Pioneer has approximately 40% market share of the U.S. seed corn business but only 2% of the world-wide seed market. Several other companies, (e.g., Dekalb, ICI Seeds, Asgrow, Funks) enjoy considerable market presence in the United States but the second largest, Dekalb Genetics Corp. has only 9% market share. Much of the seed industry (40%) is divided among hundreds of "mom-and-pop" seed companies. Many of these small companies will attempt to hold market share by exploiting niche markets and discounting prices. The larger companies (Table 6) have embarked upon an aggressive acquisition strategy to enhance their market position. The chemical industry which also followed an acquisition strategy as a means of exploiting biotechnology, may be having second thoughts about the promises claimed for biotechnology and "might pull up root soon" [4].

In forestry, vegetatively propagated materials (transplant trees) rather than seeds are the vehicle for delivery of genetic material. Production forestry in contrast to crop agriculture is highly centralized in government and industrially controlled operations. Decisions concerning the types, characteristics and the genetic material that is optimal for such opportunities are fashioned through large organizations with major internal resources to invent and develop the new technologies.

Relatively little forestry research has been done, thus there is considerable potential to increase productivity through improved disease and insect resistance. The use of clones and tissue cultures to reduce the tree breeding cycles from decades to months is producing 4 to 6-fold increases in the yields of tree crops ranging from rubber and cocoa to pulpwood [1]. Increased productivity of forests has already attracted considerable public attention as pressure mounts to retain woodlands as a reserve for endangered wildlife such as the spotted owl.

There is a range of specific opportunities for seeds perhaps best characterized by product end use.

Resistance to Pests — Plant diseases induced by fungi, bacteria and viruses result in significant reductions in agricultural production. Over $790 million of synthetic chemicals, predominately fungicides, were sold in 1992 to control plant diseases. Plants are known to contain an array of naturally occurring compounds which protect them against such diseases. Plant genetists have for years utilized natural resistance to diseases to develop resistant varieties through traditional plant breeding and have kept one step ahead in the evolution of in-

Table 6. Seed company acquisitions

Corporation	Country Base	Acquired Companies
BioTechnica	United States	Horizon, McAllister, J. M. Schult, Donley, L. Herried
Bristar	United Kingdom	W-L Research, Germains
Calgene	United States	Stoneville Pedigreed, Noble-Bear
Ciba	Switzerland	Funks Seed International
Dow/Elanco	United States	United AgriSeeds
Elf Aquitane/Sanofi	France	St. Jeannet Lasserre, Dahlgren, King Agro, Cambier Frere, Arlesa
Hoechst	Germany	Nunhems, Cannets, Hild, KWS (Minority)
ICI Seeds	United Kingdom	Garst, Societe Europeenne de Semences, Sinclair McGill, Miln Marstets, Contiseeds, and Hybrid Wheat Technology from Rohm & Haas, E. J. Funk
ITT	United States	Burpee
Limagrain	France	Ferry-Morse, Shissler, Vilmorin, Nungesser, Tezier, Picard, Nickerson (UK)
Lubrizol	United States	Agrigenetics, Sigco, Lynnville, Jacques
Monsanto	United States	Hartz, Dekalb Hybrid Wheat Program
Orsan	France	Harris-Moran, Clause (50%), Claeys, Wilson, Western Plant Breeders
Rhone-Poulenc	France	Callahan, Clause (50%), CelPril
Sandoz	Switzerland	Northrup King, Stauffer Seed, Zaadunie B.V., Rogers Brothers, Hilleshog, Cokers, Prodes, Musser, Fredonia, Vaughans
Unilever	United Kingdom/ Netherlands	PBI, Barenbrug (Majority)
Upjohn	United States	Asgrow, Os Gold, Bruinsma

* Updated from [5].

creasingly virulent strains of the disease organism. A classic example is the USDA's wheat stem rust program in the midwest. The combination of traditional plant breeding and modern biotechnology should provide greater efficiencies in that process.

Biotechnology provides the technology to insert those genes coded for virus coat proteins into plants thus conferring resistance to infection by the source virus. Virus resistance in dicotyledonous plants has been demonstrated and is likely to reach commercialization relatively soon. Viruses resistance in monocotyledons is somewhat further behind.

The molecular basis for natural resistance to insects is also known to occur in several plants. However, only limited practical applications exist today. Perhaps the best example is pyrethrum, a natural component in the flowers of Chrysanthemum. It has enjoyed over a hundred years of being used successfully where rapid knock-down and short persistency was important. Efforts to expand the biosynthesis of this insecticide in other plants would certainly open new opportunities.

The power of modern biotechnology to transmit genetic information between vastly different species has opened the prospect of introducing insecticidal properties from a bacteria, Bacillus thuringiensis (Bt), by cloning the gene coding for the toxin and inserting it into plants. The plant with the new genetic information produces its own insecticide, reducing and possibly eliminating the need for synthetic insecticidal sprays. Several major agrichemical companies are heavily involved in this activity. The U.S. market for synthetic insecticides in 1992 was estimated to be $1.39 billion.

Resistance to Chemicals —Within this category, there are at least eight known examples of genetically engineered resistance to specific herbicidal chemicals such as glyphosate and the imidazolinones. In those situations, plants normally susceptible to a specific chemical, e.g., soybeans susceptible to glyphosate, are developed utilizing a combination of techniques based on biotechnology to select and insert the gene for resistance with traditional plant breeding to establish genetic stability and guarantee that other phenotypic characteristics such as yield and oil quality are not adversely affected. Herbicides dominate the synthetic pesticide market with over $3.87 billion sold in 1992 in the United States alone.

Biotechnology offers a strategic approach to the design of novel herbicides with "ideal" properties such as appropriate persistence in the field without accumulation in ground water, effective control of a broad spectrum of weeds, absence of effects on domesticated crops, low manufacturing costs, minimal human and animal health effects, and potential for proprietariness [6]. Absence of adequate crop selectivity has in the past eliminated many candidate herbicides possessing all the other "ideal" properties. Utilizing the tools of biotechnology, it is theoretically possible to develop crop plants selectively tolerant to herbicide candidates that were initially discarded because of inadequate selectivity to crops. This reverses the traditional approach to herbicide discovery by eliminating the predominate initial requirement for crop tolerance in a random screening process.

It has been suggested that the discovery of 2,4-D in the 1930s was essentially a result of this process and has established a precedent that can be utilized today to discover novel agrichemicals. Biotechnology can be used to identify the site of action of an agrichemical. Suborganismal tests using the site of action may assist screening active structures without the confusion introduced by the processes of absorption, translocation, and metabolism in the whole organism. Directed synthesis of potential agrochemicals may be guided by knowledge of the structure of the active site of the protein target. Agrochemicals may be designed to be regulators to "turn on" or "turn off" genes at desired times. For example, such an agrichemical may be used to "turn on" pesticidal genes when pest insect populations become an economic problem.

Resistance to Cold Temperatures and Drought — These are two areas of major importance to production agriculture. Tolerance to low temperatures is a characteristic that would provide important benefits to the citrus, fruit, and winter vegetable industries. Drought resistance is an increasingly important factor as the competition for limited water supplies becomes more critical especially in the western part of the United States. Over 15% of American agriculture is grown under irrigated conditions and much of that is high-value vegetable and fruit crops. Biotechnology offers the prospect of moving genetic information between species thus offering the theoretical promise of achieving these goals. However, there has not been active research in these areas that has emerged from the laboratories, perhaps as a result of inadequate basic knowledge.

2.1.2 Microbial —The use of various microbial agents to control insects, diseases and weeds is of relatively minor importance today (the market value of all such materials is less than $70 million). They are however, gaining importance as a result of increased concerns about sustainability of agriculture and the public pressures on the synthetic materials and biotechnology provides the tools to make biological control strategies economically competitive with synthetic chemicals and fertilizers.

The most successful microbial spray to date is based on the toxin produced by Bacillus thuringiensis (Bt). It should be noted that while this is the same organism used to develop the code to insert in plants, this use is directed toward the microbe itself.

The major limitation of Bt is its narrow spectrum of susceptible insects. (This also is one of its strengths as it does not harm beneficial insects.) Commercial companies such as Mycogen Corporation have utilized genetic engineering to enhance the performance of the organism by selecting various strains of Bt that demonstrated increased toxicity to a range of insects. They genetically engineered the parent strain to incorporate the improved characteristics and have now obtained the first and to this date, the only genetically engineered microbial pesticide.

The use of genetic engineering to enhance the insecticidal properties of viruses called baculoviruses which are pathogenic toward insects such as the gypsy moth and the Heliothis and Spodoptera complexes offers significant potential to enhance a naturally occurring system. This technology is still in its infancy however, a delivery system with controlled longevity has been demonstrated suggesting considerable promise for this approach. Viable economic manufacture of the genetically engineered baculoviruses remains a significant limitation critical to their commercial use. Other potential opportunities exist for enhanced pesticidal activity by genetically modifying known herbicidal fungi and insecticidal nematodes.

2.1.3 Agrichemical—Agrichemicals have played a major role in the remarkable increases in agricultural productivity that have occurred over the past 50 years [7]. However, recent concerns about risks associated with exposure and the impact on the environment particularly non-target species have opened major opportunities for alternate or integrated strategies based on biotechnology. Improved pest control as a result of incorporating genetic modification into the seed will unquestionably reduce or alter use patterns of various agrichemicals. There is a question about how significant the downside risk may be for the agrichemical industry however, most major corporations have very active R and D programs in biotechnology suggesting they wish to be in position to participate as this technology advances. It is clear that major restructuring of the large agricultural input industries has resulted in vertical integration but how that will affect agriculture in the future is not yet clear. There are relatively new companies that are small in comparison to the major multinational companies but have already made significant contributions (e.g., Mycogen introduced the first genetically engineered microbial pesticide and Calgene is at the forefront of the genetically engineered food industry with its Flavr Savr ™ tomato).

The concerns expressed that herbicide-resistant crops will increase the use of herbicides is somewhat spurious as over 95% of the acres planted to commodity crops are currently sprayed with some type of herbicide. It is however, almost certain that herbicide-resistant crops will alter the current use patterns thus creating some winners and some losers in the agrichemical industry. One hopes the opportunities offered through biotechnology will provide the grower with more options, thus the opportunity to switch from herbicides that pose environmental risks.

Chemical pesticides and fertilizers may be viewed as "half-technologies," and genetically engineered seeds may be viewed as whole technologies. This is analogous to the view that describes pharmaceuticals as "half-technologies" and vaccines as whole technologies. Both synthetic pharmaceuticals and agrichemicals require repetitive manufacturing and use for the desired benefits; seeds are self-replicating and vaccines are used once or infrequently.

2.1.4 Fertilizer—The potential for self-fertilizing plants is immense; however, there are no practical examples that have reached the field development stage. In addition the savings in the cost of synthetic fertilizers and their application, there is a major attraction for this concept from an environmental perspective. The run-off of soil nutrients and herbicides constitutes over 60% of the non-point pollution in the United States. This source of pollution has come under increased attention from Congress which is almost certainly going to place constraints on the traditional use of these agricultural input materials. This is a major opportunity for biotechnology worth many millions of dollars. An effective system would of course have a corresponding downside impact on the sale of fertilizers.

2.1.5 Diagnostics—Increased consumer concerns about food safety and general awareness of the environment has opened up opportunities for monitoring chemical and biological resides and analyzing for the presence of pathogenic organisms. The methodology is based on nucleic acid probes and monoclonal antibodies and offers new dimensions in sensitivity and relative simplicity and speed thus suggesting major promise for the future.

This is an area which has significant theoretical potential based on the prospects of both sensitivity and simplicity in the methodology however, there has been relatively little commercial development to date.

2.1.6 Equipment/Irrigation—Wide range of values depending upon the degree of drought resistance incorporated into the plant.

As mentioned, drought resistance offers important potential opportunities especially in the 15% of American agriculture which is irrigated. The increasing scarcity of water especially in California, and the increasing concerns over water quality both will act in concert to drive up the cost of water which is already at premium levels. The impact of this characteristic will depend upon the extent of the enhanced resistance.

2.2 Production Agriculture

The primary need of farmers of the 1990's and beyond will be increased productivity — to maintain or increase market share for commodity products such as corn, soybeans, and wheat. Productivity is the key to maintaining market share in any non-subsidized commodity area. There seems little doubt, the subsidies which American and European farmers have enjoyed, will be reduced and possibly even eliminated within the next few years. This would increase even further the importance of improved productivity resulting from the consolidation of agrichemical and fertilizer inputs into seed inputs.

Crop agriculture in much of the developed world, especially the corn belt of the United States, is capable of producing far more grain than is needed within the United States or can be sold abroad. The 1980s witnessed hugh grain excesses and government programs (PIK payment-in-kind and CRP — Conservation Reserve Program) that sought to decrease grain production. A major priority in USDA is to seek new opportunities for non-traditional markets thus increasing the size of the total market for farm products. These new opportunities include chemicals, polymers, and fuels. Attempts have been made in these areas in the 1980's but most have been uneconomic in part because the characteristics of the crops being used were not tailored to fit these new, non-food opportunities use but rather, were traditional grain crops such as corn which was designed as a food/feed crop. Biotechnology offers an opportunity to reassess this position.

Modern agricultural production suffers from a perception that the systems in use today are less sustainable than many believe desirable. Biotechnology as a biologically based strategy offers the prospect of developing systems that can be sustained for long periods of time and that at the same time are profitable, environmentally friendly, conserve both renewable and non-renewable resources and meet both consumer and social needs.

A major need for producers of commodity grains and fiber is increased productivity so they can be the low-cost producer. This need for high productivity is relevant to any commodity, not just grains. Transgenic plants should enhance the efficiency of improving productivity by facilitating the breeding process and by expanding the genes available to the breeder. Farmers and countries utilizing transgenic plant products with improved productivity for commodity grains and fiber will be more profitable and competitive and will gain world market share at the expense of the less productive farmers and countries (in the absence of protection and subsidization).

The probable first commercial transgenic crop with improved productivity will be cotton that produces the Bt insect toxin for protection against pest insects. Monsanto's 1990 field trials at multiple sites in the United States [8] provided evidence that transgenic Bt cotton was as effectively protected from insect damage as cotton sprayed with multiple chemical pesticide treatments. The costs of production is expected to be less for purchase of the transgenic Bt seed than for the purchase of the traditional seed plus chemical pesticides and the cost of the multiple applications of the chemical pesticides. The cost of the transgenic seed will be greater than the traditional seed; this additional seed cost may be about 25–50% of the savings in purchased pesticides and their application cost.

Other transgenic plants with potential improved productivity are disease-resistant plants and herbicide-tolerant crops. The latter may decrease the cost of weed control by decreasing the total cost for herbicides and their application or increasing crop yields by increasing the effectiveness of weed control. The development of herbicide-tolerant crops will also provide the farmer with an increased range of options. Alternative strategies will become increasingly important with increasing public and regulatory pressures to eliminate herbicides implicated in ground-water contamination.

One of the largest opportunities for improved productivity will be self-fertilizing transgenic crops that eliminate the costs for synthetic nitrogen fertilizer and its application. While cost considerations are certainly important, rising pressures to control non-point pollution sources such as the agricultural use of fertilizers will place additional pressure on strategies based on transgenic plants.

2.3 Increased Value-in-Use Foods and Feeds

There are two aspects concerning the improved value-in-use of plant products. One is the increase in one or possibly two components of a commodity crop such as corn. The second is to enhance a specified characteristic such as flavor in the product purchased by the consumer e.g., the fresh tomato. Each case presents a unique set conditions or problems but it is likely value-in-use crops would increase profitability at all steps of production, marketing, and use.

Number 2 yellow corn is the dominant corn of commerce and is the basis for pricing of this commodity [9]. It is used in many ways in U.S. industry, e.g., livestock-feeding (55%), grain exporting (29%), wet milling (13%) and dry milling (3%) [10]. Many of these can be further segmented; for example, corn is used in livestock feed, including poultry and swine feed. The composition of corn for high value as a poultry feed is different from that for high value as a swine feed. The composition of corn with most value for wet milling is substantially different from that for livestock feeding. Thus, a plant product of a given composition can have different value, dependent upon the use to which it is put. At this time, most grain products, such as number 2 yellow corn, are treated in commerce as commodities with their price unrelated to their value in a specific use.

A primary factor is the complex nature of the sources (e.g., number 2 yellow corn is grown by many different farmers under a wide range of conditions), and the distribution channels (e.g., number 2 yellow corn is collected, mixed and stored under widely different circumstances across the country) which make it extremely difficult to identify different lots with different characteristics once they have entered the distribution network.

Commodities with improved value-in-use for a specific end use, e.g., corn with a nutritional composition that makes it more valuable than traditional number 2 yellow corn for swine production, will need to have its identity preserved throughout its production, the complex distribution process, marketing, and use. Such identity-preserved corn with increased value for swine production will be sold at a price based on its value-in-use as a feed for swine and not at a commodity price. Initially, this will require a considerable enhancement in the value-in-use as the estimated costs to alter the current distribution systems are immense.

One significant recent major commercial example of an improved value-in-use crop with identity preservation is the rapeseed crop called canola. Canola oil has higher value-in-use as an edible oil than rapeseed oil; its identity is preserved by the name "canola" rather than "rapeseed." Canola is a variety of rapeseed which Canadian scientists modified by traditional plant breeding to reduce the erucic acid and glucosinolate content so its oil was suitable for edible uses and the meal as an animal feed. Canola oil has become the dominant edible oil in Canada and recently, the United States (FDA) recognized canola oil as GRAS (generally recognized as safe). Procter and Gamble's Puritan Oil is a canola oil and is being marketed as a more healthful material because of its reduced fatty acid composition and its lighter color as a frying oil as compared to the traditional vegetable oils from corn and soybeans.

Commodity pricing in the fruit and vegetable market is common when there is mixing of like items (e.g., tomatoes) from multiple sources. Exceptions to a commodity pricing approach occur frequently in fruit and vegetable production and marketing for example, when a processor contracts with a grower to produce a specific plant under a specific set of circumstances (e.g., prescribed agrichemicals) with value for the processor's market and that product carries a specific, recognized brand label. Labelling in the banana and coffee industries are perhaps the most widely recognized examples of this.

Interest is now developing in creating identity-preserved crops so as to capture the improved value-in-use of the crop. The developers of the Flavr Savr tomato plan to identify the individual tomato so the consumer can identify and select the tomato with the antisence gene and the longer shelf life.

Calgene is developing a transgenic tomato which has a longer shelf life [11] and is targeted for the fresh fruit market which is 60% of the 500,000 acres of tomatoes grown annually in the United States. USDA concluded that while it has components derived from plant pests (the promoter used to direct expression in the Flavr Savr is a gene derived from cauliflower mosaic virus) Flavr Savr does not constitute a plant pest. This is the first food crop that USDA has approved and is likely to be the first example of a higher value-in-use crop approved by FDA which has been reviewing a Calgene request for an advisory opinion submitted August 12, 1991.

Other changes with consumer value include enhanced color, taste, flavor, and texture; ease of preparation, improved nutritional characteristics and health (e.g., reduced levels or absence of natural toxins or increased levels of beneficial antioxidants). Today's consumer is more interested in product value than cost and is prepared to pay a premium for a higher value-in-use than for a commodity.

The combination of identity preservation and pricing based on value-in-use may provide one of the largest commercial opportunities for transgenic plant products. Proprietariness as discussed below is necessary for pricing based on value-in-use. Pricing based on value-in-use will provide farmers the opportunity to produce more profitable crops. Value-in-use is key to the high profit, lower volume specialty producer while productivity is key to the low profit, high volume commodity producer. The move to identity preservation and value-in-use pricing probably will be the next major advance in crop agriculture. Proprietariness, identity preservation, and transgenic plants are the keys to value-in-use plant products.

Identity-preserved crops, in many cases, will require a reliable, rapid, and low-cost system to enable identification of the crop as it is bought and sold in commerce. A transgenic plant or its seed, with enhanced value for a specific use, will probably be identical in appearance to the commodity plant. For example, corn with enhanced nutritional value as a feed for swine will probably by visually identical to number 2 yellow corn. A marker will be needed to enable the enhanced nutritional value corn to be segregated during steps in commerce. Marker systems such as light emissions from incorporating the lux AB genes for bioluminescence may be useful [12]. There will need to be marker systems for each of the variants of a given crop whose identity is to be preserved in commerce. This need has not been solved at this time.

2.4 Non-Traditional and New Use Markets

Developed country agriculture suffers from its excess capacity, basically excess arable land which enables it to produce commodity grains in excess of the food and feed needs of the developed world and the ability of the developing world to purchase. New, non-food and feed markets are needed for plant products. Already plants have major established non-food and feed markets. These include materials (e.g., lumber), fiber (e.g., cotton, pulp, and paper), energy (e.g., ethanol for fuel alcohol, "gasohol"), industrial chemicals (e.g., acetic acid) and specialty chemicals (e.g., pharmaceuticals or pharmaceutical precursors). Some of the above needs are commodity and the opportunity is massive in size, e.g., an alcohol fuel. A major need in cases such as gasohol and chemical feedstocks is to modify plants and/or the processing of plants products to make them economical sources for those needs that now use mainly fossil energy. Successful field trials have been conducted with canola that has been genetically modified to produce industrial oils and lauric acid, a raw material for soaps, detergents, and cosmetics.

Another similar opportunity is the enhancement of the production of various components such as starch—a process which could be considered as either a nutritional or non-food production opportunity. Monsanto, for example, is attempting to increase the starch content by as much as 35% to 60% over non-engineered crops such as potatoes and corn. These higher levels could enhance the viability of producing bioethanol as a source of energy.

In the non-commodity arena, one finds high value-in-use and low volumes such as pharmaceuticals or their precursors. Some are evaluating the "manufacture" of protein therapeutics in transgenic plants. These demand a relatively high product value as the process generates relatively low yields as a percentage of the starting ingredients.

Transgenic processes will be more efficacious than traditional breeding processes thus opening many opportunities for producing plants with improved value-in-use in non-traditional markets. For example, the potential exists to produce vanilla (estimated to have a market potential of $250 million) and through the use of cell cultivars, to produce coconut and palm oils (estimated to have a market potential that might exceed $2 billion).

Companies are also exploring the possibilities of producing natural pyrethrum (estimated market value of $100 million in the United States). Alternatively, superior oils for industrial uses are being developed by Calgene [13].

3.1 Environmentally Neutral Opportunities

A growing need of crop-production agriculture is the availability of practices that are more environment neutral or compatible with sustainable crop agriculture than existing practices. The extensive use of fertilizers, especially synthetic nitrogen fertilizer, and of agrichemicals has in some cases resulted in contamination of groundwater and soils. Many expect that transgenic plants, able to make their own biodegradable biopesticides and fix their own nitrogen, will enable crop-production practices that are more environment neutral and compatible with sustainable crop agriculture. However, the use of transgenic plants to meet these needs will be based on economic considerations that relate to productivity or value-in-use of products rather than environment neutrality unless regulations require the use of the transgenic pesticidal or self-fertilizing plants rather than the application of synthetic chemicals.

The anticipated size of the commercial opportunities for transgenic plant products will be in decreasing order: expanded non-food and non-feed uses > improved value-in-use > improved productivity. It is difficult to assign commercial values to environmentally neutral crop production practices other than to incorporate them across each of the above opportunities. The time-lag prior to commercialization is expected to be the shortest for improved value-in-use (the Flavr Savr tomato was submitted for FDA in August 1991 and is expected to reach the marketplace before the end of 1993; no other transgenic plant applications are before FDA) and longest for expended, non-food and non-feed uses. Overall, transgenic plants are expected to make major contributions to all of the above needs. Commercialization in all cases will benefit from strong protection of the intellectual property associated with transgenic plants.

4.1 Status of Key Technologies Including Needs

Three technology components are necessary for commercialization of transgenic plants and products. These are 1) state-of-the-art germ plasm of host plants, 2) technology for adequate yield plant transformations, and 3) commercially useful genes. The starting material is state-of-the-art germ plasm of the domesticated crop to be improved by molecular genetic modification. This germ plasm must have proven commercial competitiveness and stability so that the transgenic modification will improve upon the germ plasm in commerce. In many cases, this state-of-the-art germ plasm is proprietary to established seed companies or companies called foundation seed companies whose business is to develop and license germ plasm to seed companies who may not develop their own germ plasm. Companies entering the seed business must develop state-of-the-art germ plasm or acquire it.

There are a variety of technologies that yield adequate transformations of many crop plants. Monsanto pioneered the use of the disarmed Agrobacterium tumefaciens plasmid for soybean, cotton, cucumber, and many other plants. Cornell invented microprojectile technology for plant transformation [14] and licensed the invention exclusively to DuPont (Anon. 1989). Recently these or other processes have produced successful transformations of corn and rice.

Transgenic corn is undoubtedly the most competitive commercial target for transgenic crops and one can anticipate greatly expanded developmental efforts in the next few years; however, the great untapped potential for world-wide development is rice.

Presently, the major technical constraint for commercialization of transgenic plants is the limited number of commercially useful genes. For example, the only types of insecticidal genes available for insect protection are limited to those based on Bt toxins, possibly protease inhibitors and the enhancins discovered at Boyce Thompson Institute [15]. The enhancins degrade an insect's peritrophic membrane, thereby synergizing insect kill by biopesticides that enter through the insect's gastrointestinal system. Additionally, there are eight known genes that control herbicide resistance.

For biotechnology to become successful however, the list of genes available for genetic modification must be expanded to include additional ones for uses such as disease resistance, nutritional quality flavor, color, etc. This limitation results from the inadequate support of agricultural research for several decades in contrast to the continuous, abundant, long-term support of biomedical research where many useful genes or gene products are available. Public sector research in identification of additional genes for use in making transgenic plants is critical to successful commercialization.

A comparison of the European and Japanese positions on the key technologies that underpin biotechnology with those in the United States, demonstrate that the United States enjoys a clear leadership position at this time (Table 4). The Europeans appear to have parity in plant cell culture, selectable markers and the very critical gene source technology. In the other technologies, with the exception of selectable marker technology in Japan, both Japan and Europe appear to be lagging the United States with recent gains being made by Europe in plant transformation technology. There is however, a belief that the United States could lose its leadership position in the near term if crop agriculture technology does not obtain adequate public support.

Antisense technology is a variant process that operates by "turning off" an enzyme that facilitates cell decomposition. Calgene is utilizing this technology to produce transgenic tomatoes with extended shelf life as noted above.

5.1 Proprietariness

Protection of intellectual property rights for novel living organisms such as plants, bacteria, and animals advanced in the United States during the 1980's when the economic potential of biotechnology and transgenic organisms was recognized. Prior to that time the Plant Patent Act of 1930 protected asexually propagated plants while hybrid crops such as corn contained a built-in proprietariness based on the process of seed production. Most crops, however, are not asexually propagated or hybrids and the commercial incentive for crop improvement required additional attention to assure proprietariness.

In 1970, the Plant Variety Protection Act was introduced in the United States to provide improved proprietariness for non-hybrid and non-asexually propagated crops. This act was administered by USDA and provided plant variety certificates (PVC) for novel plants. These certificates provided limited proprietariness for improved plants but did not provide the exclusivity of a patent issued by the U.S. Patent and Trademark Office (PTO) as farmers were permitted to plant and sell seed produced from purchased seed protected by a PVC. Thus, seeds with major improvements in their value might only be sold once or a competitor could make a modest improvement in a plant covered by a PVC and obtain a new PVC for a modestly improved plant. Clearly this was an inadequate system to protect against the higher costs associated with the development of transgenic plants as compared to those produced through traditional plant breeding.

During the 1980's the PTO extended proprietariness, initially to novel microorganisms, then to novel higher plants and ultimately to novel animals. The legal precedent for the patentability of genetically modified plant materials occurred in 1986 [16] with the issue of a U.S. patent for tryptophan-overproducer mutants of cereal crops [17]. Several patents have now been issued for genetically modified plants including transgenic plants.

The extension of patentability to living organisms has been in parallel with the ability to describe biological modifications in molecular rather than morphological terms. Such proprietariness is necessary to enable commercial organizations to obtain an equitable return on their research and development risk-investment consistent with the added value of the transgenic product. Since many of these transgenic crops will have global markets, it is key that appropriate proprietariness be available in, at least, the developed countries of the world. Furthermore, proprietariness of a transgenic crop product will allow each member of the product chain—e.g., agribusiness input, farmer, food/feed processor and distributor, and non-food/non-feed processor and distributor—to obtain a price consistent with the value of the product at that step and is critical to assure aggressive commercial development.

Confidential Business Information (CBI) is a related concept of proprietariness, however, because it is not protected by patents it is an extremely sensitive issue. The sensitivity is increased because of the inherent conflict between the industry generating the information and those who believe that information is requisite to making a determination of the acceptability of either health or environmental risks. On the one hand, industry is anxious to protect information which it considers proprietary for sound business reasons and usually can not be included within the scope of the patent. On the other hand, public interest advocates seek information they believe is necessary to evaluate the risks inherent in the new technology and thus maintain pressure for additional information. Conflict arises when these two forces disagree over whether specific information is CBI or required to evaluate risk.

6.1 Regulatory Aspects

There are two basic concerns related to crop agriculture and the use of biotechnology. The first concern relates to the potential impact of the release of the organism on the environment. The second concern is directed toward plants or products that will eventually become food and is directed at the issue of food safety. As they relate to two different jurisdictions with the Federal Government and fall under two different Federal Laws, they will be treated separately, however, it is important to note that the framework guiding regulatory roles and requirements is very unclear and remains a major constraint to the development of genetically engineered plant products. Organizations intending to develop such products must have a full awareness of the current regulatory status as it will have a major impact on the amount and type of information (costs) and the probable time to achieve commercialization.

7.1 Environmental Issues

The USDA under the Plant Pest Act, has the primary responsibility to oversee these aspects of genetic release and to determine whether there is a plant pest risk. They are concerned whether genetically modified organisms in any way alter the environment or whether it is possible for the genetic information to move from the genetically modified plant to an indigenous host.

The USDA has evaluated over 400 applications for a variety of plants over the past 6 years and in a March, 1993 ruling indicated they now have adequate experience to establish a notification and petition process that allows one to conduct field tests on 6 crops (corn, soybean, tobacco, tomato, cotton, and potato) without first applying for a permit from the Animal and Plant Health Inspection Service (APHIS, the regulatory arm of USDA with responsibility for regulating genetically modified plants). APHIS still requires information about the regulated article such as the donor organism for all the genes that contributed to the introduced genetic material, the method used to transform the recipient, the size of the filed test and the date and location of the release. Notification of field trials must be received by APHIS at least 30 days prior to the test and detailed follow-up reports are required annually. This is the first example in which a regulation has been modified to incorporate the experiences gained since the beginning of genetically modified plants and certainly is a welcome sign.

The regulatory aspects guiding the release of microorganisms are under the jurisdiction of EPA which regulates these under the Toxic Substances Control Act (TSCA). The regulatory status of pesticidal substances produced by plants are regulated by EPA under the Federal Insecticide, Fungicide and Rodenticide ACT (FIFRA). Neither rule has yet been finalized. The first experimental use permit (EUP) was granted by EPA to field test transgenic cotton plants altered to produce the Bt toxin derived from the soil microbe, Bacillus thuringiensis subspecies tenebrionis, for the control of certain caterpillar pests.

Pesticidal products are subject to regulation under FIFRA, 40 CFR Part 172. Genetically engineered microbial pesticides have fallen under the "Proposal for a Coordinated Framework for Regulation of Biotechnology" and all genetically altered and nonindigenous pesticides have since been subject to screening prior to their release into the environment (51 FR 23302). EPA now has experience resulting from over 75 notifications for small-scale field testing and have proposed that certain of these microbial pesticides need not be subject to screening involved in the current notification process. This is part of the effort to minimize the amount of data required for field testing and to reduce the time required for review and is consistent with the USDA's recent announcement to streamline the testing procedures mentioned above.

There is also increasing evidence of coordination between agencies, for example, EPA recently proposed that nonindigenous microbes, already subject to USDA regulation under 7 CFR 330 and the jurisdiction of APHIS will not require additional oversight from EPA. Minimization of duplication should reduce the time and paperwork required to introduce new organisms. Also encouraging is EPA's proposal eliminating the need for notification of testing microorganisms in contained facilities.

As mentioned earlier, differences of opinion remain between the amount of information the public believes it needs to have to determine acceptability and the confidentiality of business information that industry believes it must retain to insure it retains a proprietary position. This debate is likely to continue for some time and companies will have to give considerable thought about what information can and should be released. This is particularly important if the information is critical to the success of the product and the company is in a start-up configuration and has no other products.

EPA has also introduced the notion of voluntary submissions in those cases where uncertainty exists concerning the need for notification. It is also advised by FDA that in the case of uncertainty, the applicant discusses the details with the Agency. Clearly, one is well advised to interact with the Agency at the earliest possible time in the development sequence to obtain appropriate guidance. Even with clear guidelines, given that biotechnology is still very new and also that there is high level of public scrutiny, one is well advised to open a dialog with the appropriate Agency if there any questions concerning the applicability of the rules.

It is also important to remember that the rules are subject to modification at almost any time. For example, there is under consideration a mechanism to propose potential exemptions from some of the above environmental regulations. Organisms that could be covered would pose no greater risk in terms of competitiveness or survivability than their unmodified counterparts. Such exemptions could, if approved, apply to constructs of Bt where only the DNA from other strains of Bt were transferred to the recipient. Again, to avoid unnecessary expense and time, one is advised to maintain close contact with the regulatory agencies.

8.1 Food Safety Issues

The second aspect of the regulatory oversight is that of food safety. This has been an area of extreme controversy and one that is likely to require more time before it is fully resolved. Obviously, it is of critical importance to those who are in the process of developing genetically modified foods for the consumer market.

The major issues are involved with the question of how to evaluate foods which result from genetic modifications utilizing the modern techniques of biotechnology. For example, are genetically engineered tomatoes with reduced enzymatic activity that have, as a consequence, an improved shelf-life significantly different from the tomatoes developed using traditional plant breeding techniques and, if so, what level of regulation is required? A corollary question is should products resulting from modern genetic engineering be required to have a label that indicates the process used to achieve the product.

These questions reflect the nearly decade-old debate over process versus product driven regulations and may be viewed from another perspective—when does the process of genetic modification result in a product that is sufficiently different to warrant concern by the regulatory body (FDA in this case of food safety)? A rational argument suggests that the genetic makeup of plants and indeed of all organisms has been subject to genetic transformation since the beginning of biological time, i.e., when the nucleic code had sufficient integrity so that any modification of the genetic code induced change. Indeed, it is those very modifications (mutations) which have resulted in the evolution of the millions of plant and animal species in existence today.

The fact that portions of the genetic code can be moved between species, the power of modern biotechnology, has initiated concerns that traditional characteristics could be modified without apparent oversight and control and that unacceptable risks might occur as a result of these transformations.

Such were the concerns of a panel of esteemed genetists, biologists and food experts that spent over 2 years evaluating the potential outcomes brought about by utilizing modern biotechnology in the development of new foods. The report of the group, IFBC [18], is the basis for the proposed rule published by FDA in May, 1992.

Publication of this rule generated significant responses from the public and as a result, FDA has recently reopened the comment period to consider a possible notification process and a public discussion of the various options surrounding product labelling.

The public debate is primarily focused around the labelling question—Should food products derived through modern biotechnology (e.g., recombinate DNA and cellular infusion techniques) be labelled simply because of the process by which they were derived or should regulatory oversight be directed toward those characteristics of the product which are in fact different (e.g., major changes in a nutritive component, the introduction of an allergenic protein)?

While not exhaustive, these are some aspects of the debate over the rules which will govern how products derived from modern biotechnology will be evaluated and the amount and type of information that will be required before the product reaches the marketplace. As a potential developer of a food product based upon recombinant DNA, for example, one must be prepared to endure a lengthy and expensive process in bringing such products to the market certainly for the next few years as the first food product has yet to clear the regulatory hurdle.

There is considerable disarray in the International regulatory arena concerning biotechnology. The European Community for example, is faced with the prospect of dealing with process oriented regulations and the so-called fourth hurdle which would place socio-economic barriers in the development of products. Such barriers are extremely difficult to comply with. They also present opportunities as many organizations do not wish to cope with such regulations.

9.1 Limitations and Constraints

9.2 Science/Technology—The major constraint related to the science of biotechnology is the basic inability to provide beneficial genes. There are only limited numbers available and until others are discovered, the future is somewhat limited. This lack of basic knowledge will likely be overcome with publicly funded research. No such limitations are evident in the biomedical world which has received substantially larger sums for research that agriculture.

Currently, the United States enjoys overall technical leadership in the science of biotechnology but there are areas of parity and given the Japanese desire to take the leadership role, the United States position could be jeopardy.

9.3 Financial—The health care and pharmaceutical components of the stock market have run some 200% ahead of the financial gains represented by the Standard and Poor's average of 500 stocks whereas the agricultural component is running 20% behind the same average. While such figures are difficult to assess accurately, suffice it to say the financial markets have clearly supported and benefitted the health care industries. Financial support for the crop agricultural markets undoubtedly will become increasingly difficult as time passes before any major product appears in the market, an event highly dependent upon appropriate resolution of the regulatory questions.

9.4 Regulatory—The critical issues are those of pre-market notification and labelling. These must be resolved before genetically engineered foods enter the market place.

9.5 Patent Coverage and Litigation—This issue appears to have been resolved with the recent modifications to the international diversity treaty as proposed by the biotechnology industry.

9.6 Consumer/Society Acceptance—This remains the key constraint to the progress of the products of biotechnology to the marketplace. The primary reason appears the lack of understanding on the part of the general public about the precise nature of what constitutes genetically engineered food. Consequently, they have an innate fear of the safety. The public also has a sense of mistrust concerning the scientist and the impact of technology on the average person. These concerns are driven by the public perception of excessive risks associated with such technologies as nuclear energy and synthetic chemicals such as pesticides.

There is also reluctance to visualize and accept the potential benefits of biotechnology. Rather, it is perceived as a means to profitable ends for big business and not for the "man on the street." Of course the average American is relatively well fed and does not have the same concerns about where the next meal is coming from that much of the third world has today and will have even more so as the population demands an increased food supply.

The public will likely demand the opportunity to make choices between what it perceives as a less risky option. Until it is sure the risks are relatively small and that it perceives an adequate benefit, one must expect the public to continue the *status quo*. The role of public values and its perception of risk will be fundamental to the future of crop biotechnology.

10.1 Summary

Dr. Vernon Ruttan [19] perhaps summarized the status of Crop Agriculture best when he said, "the capacity of American agriculture to expand its foreign markets depends on continued declines in the real costs of production. American agriculture has achieved its preeminence in the world by substituting knowledge for resources. This knowledge, embodied in more productive biological, chemical, and mechanical technologies and the management skills of farm operators, has given the United States a world-class agricultural industry at a time when many other sectors of the economy are losing their preeminent position. A necessary condition for U.S. agriculture to retain its status is enhancement of both public and private sector capacity for scientific research and technology development. The costs, to both consumers and producers of failure to maintain and enhance our efficiency in production would greatly exceed the adjustment costs resulting from abundance."

It is clear from Dr. Ruttan's statements and the above discussion, there is a fundamental need to support additional basic research. It is also evident that before the products of biotechnology can reach the marketplace, there must be clear and credible regulatory guidance that will allow on the one hand the products to move forward while at the same time assuring the public that there are not unreasonable health and environmental risks associated with the products of modern biotechnology.

Modern biotechnology offers the prospect of 1) increasing agricultural productivity at a time when the population of the world is about to double; 2) improve the opportunities to improve global competitiveness at a time when crop subsidies are under tremendous pressure and may even disappear; 3) enhancing the environment at a time when environmental concerns about such issues as pesticide exposure and groundwater contamination are rising; and 4) improve food safety and quality at a time when issues such as pesticide residues and nutrition are highly visible to the consumer. Given these prospects, it is imperative that the general public and their elected representatives endorse modern biotechnology and its products—an endorsement that will have to be earned and reasonably soon.

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Ralph W. F. Hardy has spent almost all of his professional career in the private sector, both for profit and not-for-profit, and during the last 2 decades has been involved in management and in advisory boards in biotechnology. From 1974–84 he was Associate Director and then Director of Life Sciences at DuPont where he established the DuPont biotechnology program for health care, agriculture/food, and chemicals. From 1984–1990 he was President and Deputy Chairman of BioTechnica where he established two affiliate companies and continues as a consultant and a member of the Board of Directors. From 1986 to the present he has been President and CEO of Boyce Thompson Institute for Plant Research Inc. where he has expanded the role of biotechnology in the discovery of biological alternatives to pesticides and fertilizer nitrogen and the definition of global environmental problems and creation of options for their minimization. He is or has been a member of several National Research Council Commissions, Boards, and Committees; a member of advisory committees to the Department of Energy; and a member of the newly created Alternative Agricultural Research and Commercialization Board of the Department of Agriculture, formed to promote new uses for agricultural materials. He was a board member of the Industrial Biotechnology Association, the trade organization for biotechnology. He is the co-founder and Chairman of the National Agricultural Biotechnology Council.

Richard A. Herrett, after an initial period as a Senior Scientist at the Boyce Thompson Institute for Plant Research, spent his professional career in private industry. Initially, he was responsible for the discovery and development of novel agrichemicals for Union Carbide Corporation. He moved to ICI in 1970 and established their R and D facilities and programs in the United States. In 1987, he moved from Director of Research and Development to Scientific Liaison in Government Relations until his retirement in 1992 at which time, he established EnvirAg Associates, a consulting firm that specializes in agricultural and environmental issues.

Dr. Herrett is currently treasurer and a member of the Executive Board of the North Carolina Biotechnology Center. He was a member of the Board of Directors and Chairman of the Agriculture and Environment Committee of the Association of Biotechnology Companies (ABC) prior to the merger and now serves on the Management Committee of the Agriculture Council of the newly merged BIO. He was previously a Member of the Board of the Agricultural Research Institute and served as Chairman of the Research Directors Committee of the National Agricultural Chemicals Association. In 1984, he worked with the National Academy of Sciences to establish a Center of Excellence in Biotechnology for Thailand.

Innovative Opportunities in Animal Biotechnology

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Production animal agriculture provides the major source of food for the United States and other portions of the world. In addition to bringing food to market, the companies responsible for processing animals also supply wool, leather, and special materials for further industrial applications. The goal of the animal industry is the more efficient utilization of resources into food and animal products. This can be accomplished by 1) increasing the conversion efficiency of feed to meat (protein yield), 2) improving the health of the production animal, and 3) improving the composition of the final consumer product. Since earliest times these improvements and advances were made by traditional breeding and classical technology. The increase in understanding the molecular basis of genetics and the means by which we can modify the genetic makeup of organisms has set the stage for dramatic changes in the production of animals and animal products. Applying the tools of biotechnology has signaled major advances in the goals for the animal and food industry. Research in reproductive technology, production enhancers, and new transgenic animals with improved production traits will increase production by allowing more efficient conversion of natural resources into meat and fiber. The greatest opportunities for research and development exist in applying genetic engineering to the development of new products for animal health. Utilizing an array of DNA manipulations, new vaccines, diagnostics and immunotherapeutics are now available to the animal industry. The final consumer food products are continually being improved by sophisticated genetic engineering. These advances include bioprocessing, enzyme technology, and transgenic manipulations. Looming on the scene is the use of farm animals for the production of specialty biochemicals. More precisely, certain extremely valuable human biologicals (pharmaceuticals) can be safely and efficiently manufactured in transgenic animals. Significant marketing opportunities can be realized by using biotechnology to provide new health products for use in companion animals (pets). The obstacles to bringing new biotechnology products to market are significant. The major difficulties on the road to commercializing include 1) technical challenges, 2) regulatory hurdles, 3) competition, 4) consumer education and acceptance, 5) activist resistance, and 6) quality manufacturing issues.ts to market are significant. The major difficulties on the road to commercializing include 1) technical challenges, 2) regulatory hurdles, 3) competition, 4) consumer education and acceptance, 5) activist resistance, and 6) quality manufacturing issues.

1. Introduction

Genetic engineering and biotechnology are words and phrases that are used by the public at large and the media to describe the "New Biology." This new biology is founded in the old science of fermentation and has evolved with the introduction of new understanding and applications of the genetics of organisms.

Fermentation has, over the last few thousands of years, given us beer, wine, bread and more recently penicillin. This technology has become very commonplace and well accepted. Beginning in the 1950's and growing in impetus in the 1970's, an increased understanding of the molecular basis for heredity and the means by which we can modify the genetic make up of organisms in a directed and controlled fashion has been developing. These evolving techniques have been used by a variety of scientists to develop new products and as research tools to better understand the basis for biological phenomena.

These new technologies and techniques have had broad applications including those in the area of animal biology, the focus for this chapter. The animal biology area is not a narrow application but rather a broad based array of potential. The array includes the application of the technology for a more efficient production of a safe, affordable and plentiful food supply. It is often forgotten that the processing of animals supplies us with specialty products for industrial applications and fibers such as wool and leather. Improvements in the production of animals will be reflected in the quality and quantity of these end products and will be beneficial to the ultimate consumer.

Thus, the new tools and techniques of biotechnology can be directed to improving the health of the producing animal. Technological advancements in vaccines and immunotherapeutics are a direct result of the New Biology. With a better understanding of the diseased state, it has been possible to develop improved, highly sensitive and reliable diagnostic tests which can determine the incidence and the extent of disease in farm animals. These technologies will have a direct impact on the cost of production as well as the safety of the end result, the food.

Secondly, the application of genetic engineering and manufacturing by sophisticated bioengineering has led to products for increasing the conversion efficiency of feed to food. Some of these production enhancers are ready for market.

The third application of biotechnology encompasses improving the composition of animal food products. These market driven conversions of post-production animal products are only briefly discussed in this chapter. Food safety and environmental issues are a vital concern to the animal industry. Fortunately the tools of biotechnology can readily address these concerns.

Not only do animals supply us with food and fiber, but also a wide array of specialty chemicals. These chemicals are characterized by their high price compared with the commodity foods and fibers. These specialty chemicals include pharmaceuticals for human use. An offshoot of this area is the development of transgenic animals, where the genetic make-up of the animal has been modified so that the animal produces a high priced pharmaceutical which it would not normally produce. These transgenic animals have been referred to as "Pharm" animals.

An important area which utilizes genetic engineering and biotechnology is the companion animal (pet) industry. This encompasses the development of directed pet breeding, as well as pharmaceuticals and diagnostics for pet diseases.

This review does not intend to cover all the applications of the technology in complete detail, but rather intends to use some specific examples to illustrate the various opportunities and issues that the novices in the area might be exposed to as they develop new product concepts and attempt to introduce them into the market. For those entrepreneurs involved in early development or the research phase of discovery an understanding of potential roadblocks and issues should be gained from this review.

Each specific area will define its special set of challenges that need to be addressed. It is clear that certain areas do pose less of a challenge than others but the common threads of regulatory issues, public perception, and economic challenges are shown by all. While a snapshot of the issues impacting the technology today can be described, the one certainty is that the situation can and will change over the life of the product from inception to marketing. The agile developer must maintain cognizance of the issues.

2. Research and Development Opportunities in Animal Health

In the United States 67% of the protein in our diet comes from animals and their products. On a world wide basis animals provide 35% of dietary protein. Meat, milk, poultry, and aquatic animals contribute most of the calcium, phosphorus and many essential vitamins so important to our diets. Over half of U.S. agriculture's annual income of $83.7 billion (1989) comes from livestock and poultry products. Sizable portions of the grain grown in the United States are consumed by livestock: approximately 87% of the corn, 95% of the grain sorghums. It is to be noted that the grasses and forage, including forage on land not tillable for other crops, is utilized by livestock for ultimate production of food and fiber.

Proper management of animals, whether livestock and poultry, companion pets, or laboratory animals, requires 1) proper nutrition or dietary procedures, 2) appropriate facilities and 3) maintenance of healthy conditions. The key word in all of this is management. Long term investment in research and development (from both government and industry sources) provides excellent opportunities for profitable large scale animal production in the United States and many other areas of the globe. Knowledgeable owners of pets provide responsible treatment of very important companion animals.

Animal health problems account for about $16.7 billion in losses each year to the American farmer. This loss affects the American consumer through lowered supplies of food and higher prices. The American consumer also wants foods that are free of toxic chemical residues and harmful microbial contaminants. Healthy farm animals must receive proper diets and live in environments that are free of toxic residues and contamination by infectious agents which otherwise might enter the food chain. It is to these goals that opportunities in biotechnology research and development have led to new and effective products which provide for the health of animals.

The total animal health market is estimated to be about $3.2 billion per year in the United States, $2.4 billion in Europe. Including the rest of the world the total figure is close to $10 billion annually. Since animal agriculture is so valuable, research on animal health is critically important. Healthy animals and poultry are necessary to maximize their genetic potential to use feed for efficient growth, reproduction and performance.

Opportunities also exist in the area of companion animals. Currently in the United States there are 50 million dogs, 5 million horses, and 67 million cats. Exotic birds and fish have always been important companion animals. Zoos and protected environments have become important repositories of endangered animal species. Consideration of providing for the health and longevity of companion animals and protected animals is a significant market for animal health care products.

2.1 Animal Health Product Development

Biotechnology yields its greatest innovative opportunities in the commercialization of new and effective products for the animal health industry.

Various bacterial, viral, fungal and parasitic infectious diseases take a significant toll in animal production. This consists of 1) death of the animal, 2) reproductive losses, 3) loss of the newborn, and 4) loss of productivity or performance.

These infectious agent problems are countered by 1) vaccination with specific protective immunogens to prevent the establishment of the disease agent in the host animal, 2) application of immune therapeutics and/or antibiotics to treat established infection, 3) genetic manipulation of the host to establish genetic resistance to disease, 4) sound management procedures to limit infectious exposure (may include USDA eradication and control programs) and to prevent stress. Proper nutrition is an important component of disease management.

Feedlot and dairy operators carry out continual risk benefit analysis in that they must decide which counter measures against infectious disease to implement for livestock and milk production. Prevention risk/loss figures become significant for successful management. They must balance projected (calculated expectations) loss figures against the dollar figures for counter measures. In some cases the labor and time figures become significant.

Antibiotics are costly for use in livestock and poultry. Prolonged continuous use can lead to the establishment of resistant strains that may become serious production problems as well as human medical problems. The federal and state requirements limiting the allowable antibiotic residues in meat and milk have increased. Thus technological opportunities come to the forefront in devising innovative methods of disease control without antibiotics in livestock and dairy operations.

2.2 Vaccines

The specific products for combating infectious disease in animals may be considered as anti-infectives. These products include vaccines and immunotherapeutics. This is the arena of countering problems of infectious disease by targeting the immune system of the host animal. Other antimicrobial products include probiotics and, of course, antibiotics.

Active vaccination countermeasures consist of: 1) immunizing the host to prevent subsequent infection upon exposure to the respective microorganisms (protective immunity), 2) using certain immunomodulators as anti-infectives for the elimination of the effects of the disease (immunotherapeutic treatment).

Establishing the virulent pathogenic strain of an organism usually provides the strain of choice for research and development of an effective vaccine. Virulence factors in the pathogenic strains usually provide clues for developing an effective vaccine or protective immunogen. The classical steps have been: 1) isolate the pathogen from the host, 2) characterize the pathogen, and 3) determine the course of infection in the host (or hosts) and observe the immune mechanisms involved in the progression of the disease.

Traditional immunization procedures consist of antigenic stimulation of antibodies and memory B cells. Specific antibodies would remain in the host after the initial presentation of an effective immunogenic determinant. If an infectious antigen became present in the host then the B cells would remember the determinants and mount a series of immune reactions to eliminate the invading infectious agent.

The mechanism of live avirulent strains as protective immunogens triggers off immune mechanisms involving not only B cells but also T cell and macrophages. The activation of these components of the cell mediated immune system in conjunction with the MHC (Major Histocompatibility Complex) 1 and MHC II reception sites can lead to a very effective response in reaction to a potential infectious state. Moreover, effective stimulation of this chain of events with memory cells can provide much more long lasting immunity (ideally for the life of the animal).

Viral, bacterial, fungal, and protozoic organisms cause diseases in livestock and poultry. Categories of vaccines to prevent the infections caused by these agents consist of: 1) killed (inactivated) organisms, 2) subunit, 3) live but attenuated, and 4) vectors. Subunit vaccines consist of immunogenic components obtained or derived from the infectious agent. These components maybe produced by recombinant DNA procedures. Attenuated vaccines may be obtained by classical modification techniques or developed by genetic engineering procedures. Vector vaccines are genetically engineered microorganisms which serve as vector agents and contain the protective immunogen from another organism.

An example of a vaccine utilizing an immunogenic component obtained by recombinant DNA procedures is the vaccine for protection against human Hepatitis B virus. This is a recombinant protein cloned from Hepatitis B virus and produced in yeast. This provides for an immune response to a protein determinant (immunogen) which can be produced without other suspected animal viruses contaminating the production.

This type of technology is extremely desirable for many vaccines including those for use in the livestock and poultry industry. The advantages are: 1) manufacturing becomes low risk, i.e., bioprocessing the antigen (immunogen) in yeast or *E. Coli* is much safer for manufacturing personnel, 2) the procedure yields an extremely pure product, (This is fine if the pure product provides the desired immunity in the host), 3) the final product is extremely safe for the immunized host, and 4) the product is cost effective.

Genetically engineered bacterial vaccines are under development for the control of bovine brucellosis. *Brucella abortus* is an intracellular pathogen of the bovine reproductive system and under certain circumstances can evade the immune surveillance system in the host animal. *Brucella abortus* is also a human pathogen, and this factor provides added incentive to develop new vaccines. Additionally, wildlife ruminants and wild pigs can become reservoirs of infection.

Effective killed vaccine for use in the United States are simply not obtainable. Killed Brucella abortus vaccines designed to stimulate humoral (B Cell) responses in bovine have not been shown to provide significant protection. Some of the killed vaccines provide protection for only 6 months and the amount of immunogenic material in conjunction with a chosen adjuvant can provide a lingering necrotic lesion. Such vaccination arrangement may be effective in closed herds in the European beef and dairy operations, but do not meet the livestock herd management requirements in the United States.

The requirements for an effective protective vaccine for the control, surveillance, and eradication of brucellosis from the beef and dairy operations in the United States are: 1) provide lifetime protection for animal, 2) the live vaccine needs to be avirulent, but also effective, 3) essentially safe if inadvertently injected by the veterinarians or escapes to the wild life populations, 4) serologically distinguishable from the field strain organism i.e., this means the vaccine strain must contain an insert (or deletion marker) that is detectable with readily applicable diagnostic tests, and 5) cost effective for the economics of the industry. Several vaccines meeting these criteria are currently being tested for use in the bovine herds in this country.

Technical advances in cloning and gene expression have led to the evolution of the recombinant DNA vector vaccines. Successful examples of such a vaccine include using the vaccinia virus for carrying an insert of the particular immunogens for countering rabies infection in wildlife. A similar vaccine using vaccinia as a vector for controlling rinderpest in Africa is nearing the large scale test stage.

Another example of genetically altered organisms for effective control of infection is the production of avirulent *salmonella* strains. The proposed plan is to introduce the genetically engineered avirulent strains of *salmonella* into poultry. The avirulent forms of *salmonella* would establish themselves and either do one or both of two things: 1) provide protective immunity against the pathogenic strains (i.e., operate as a living vaccine for lifetime protection of the chicken) or 2) establish the avirulent form of *salmonella* in a competitive colonizing role, thus preventing virulent forms to become the dominant strains.

Some of the requirements for applying new genetically engineered strains of *salmonella* are: 1) they must be safe, i.e., avirulent for both poultry and humans, 2) the new strains must be shown not to revert to the virulent forms, and 3) the use of these strains must be cost effective for the industry, i.e., to manufacture and to administer to broilers, laying flocks, etc.

The debilitating effects of Trypanosomiasis in semitropical regions prevent effective cattle production in large portions of Africa. The tools of biotechnology present opportunities to develop effective vaccines against this disease and other diseases caused by protozoa.

Bovine Spongiform Encephalopathy (BSE) is a progressive, fatal, nervous disease of adult domestic cattle which closely resembles scrapie of sheep and goats. The infectious agent is probably a prion. An effective vaccine is sorely needed to counter this global threat to the beef and dairy industry.

A renewal of tuberculosis problems in cattle and other ruminants always looms over the livestock industry. An effective vaccine is not available for this disease.

This is only a short listing of examples of opportunities for vaccine development. There will always be a need for new and more effective vaccines.

2.3 Diagnostics

Diagnosis of animal diseases often involves clinical examination, serologic tests, or cultural or microscopic examination of a wide spectrum of samples, fluids or tissues.

The size of the animal diagnostic market is estimated to be $50,000,000 per year. Satisfactory diagnostic tests are not available for many important diseases. The goals for a satisfactory diagnostic procedure are: 1) safe for the host animal and human workers, 2) accurate and very specific, i.e., must be able to distinguish from many pathogenic strains and organisms, 3) rapid—time is of the essence in the feedlot and for the control of organisms, 4) inexpensive—the use of diagnostics, like protective immunogens, is a function of economics, 5) easy to use, but reliable—unlike human medicine the use of diagnostic may not be by highly skilled health professionals. The area of developing new and effective diagnostic procedures is one of the best arenas for innovative opportunities in biotechnology.

Reliable and highly specific tests that can be readily performed by technical support personnel with limited training outside of laboratory facilities are in great demand. Production animals do not come into an office, but instead the production specialist would like to examine fluids via a "field test" and to know as soon as possible what the infectious agent is. Pet animals are of course brought into offices for obtaining body fluids (and examination) but an interesting area of veterinary practice that is increasing is the "vet on wheels" for small animals. (This was of course always the case for large animal practitioners.)

Molecular approaches to infectious disease diagnosis can be specifically developed for use on such varied samples as: tissues, cells, blood, urine, feces, mucosal swabs, skin scraping, semen or other specimens. The successful marketing of these new molecular agents must be compared against and be more advantageous than current conventional cultural, histopathic, microscopic or immunologic diagnostic methods. Most previous methods of diagnosis consisted of detecting circulating antibodies to the respective infectious agent using a serological procedure based upon antigen-antibody reactions. Cutting edge technology employs application of monoclonal antibodies and nucleic acid hybridization (probes), and DNA finger printing (restriction analysis).

The requirements for an immunoassay are: 1) appropriate source of antigen or specific antibody, 2) a matrix in or on which the antigen-antibody reaction will occur and, 3) a read out system to measure the extent of the reaction. Utilization of these three steps provides for the development of an effective diagnostic configuration which are usually marketed as "kits." The use of monoclonal antibodies (MAB) in combination with enzyme-linked immunosorbent assays (ELISA) has been exploited in the rapid development of diagnostic test kits. In this immunoassay technique the specific antibodies are coupled to enzymes. The respective enzymes catalyze reactions involving chromogenic changes readily detected by spectrophotometric methods.

The technology for creating monoclonal antibodies (MAB) has had a significant role in providing innovative opportunities to develop more specific (effective) assays. In this technique spleen cells producing antibodies to a target substance are fused with tumor cells. This fusion produces a hybrid cell containing the combined genetic information of both parental cells, which is capable of secreting the antibody produced by parental spleen cell and, like the parent tumor cell, can live indefinitely in culture medium. The commercial advantage of MAB is that the stable hybridoma can produce large quantities of antibodies from cell lines with unchanging capacity to produce the antigen of interest. From a manufacturing quality control perspective these MABs can provide additional benefits in terms of specificity and ease of kit and delivery design. MABs are particularly useful in the competitive assay design to measure specific antibody amounts in test sample fluid. These MAB are of particular value for USDA action, i.e., control and eradication programs, for pseudorabies and brucellosis. In these programs a vaccination regimen is implemented and specific assays are required to differentiate vaccinated animals from infected or wild type (field strains).

In addition to the hybridoma technology, the use of recombinant DNA procedure for obtaining antigen by genetic engineering becomes a cost effective means for producing immunoassay kits. These assays, designed to detect antibodies as markers for infection, require a source of antigen specific for the particular infectious agent. The production of the microorganism as a source of antigen may be difficult, costly, and present safety problems to human workers. Thus, genetic engineering procedures for the cloning of the protein (antigen) from the pathogenic organisms into an expression in *E. coli*, yeast, or mammalian cells are utilized. Examples of this technique are the production of the envelope or core protein from Feline Leukemia Virus (FLV) or Feline Immunodeficiency Virus (FIV).

The technology, capitalizing on the complimentary hybridizing properties of nucleic acid, has enabled the development of DNA probes for extremely specific detection of microorganisms. Furthermore, these DNA probes can aid in the differentiation of closely related microorganisms. Detection of the presence of specific serovar or strains can influence the therapeutic or preventive measures taken by the practitioners. Clinical samples are often complicated by the presence of nucleic acid by closely related (and non related) nonpathogens or pathogens. Those probe methods which include disruption of host tissue obviously contain significant amounts of host DNA. The total market for DNA probes (both human and veterinary) will reach over $500 million in the next 5 years.

The typing of DNA (finger printing) by restriction enzyme has other applications. These include, for example, detection of genetic defects, genome mapping, sex determination in sperm cells, paternity determination and microbial classification. To be noted are possible forensic uses and establishment of proprietary claims.

In human medicine, nucleic acid probes have been made for the detection and prognosis of certain malignancies. Some conditions have been associated with viral infections such as cervical cancer. Certain leukemias and lymphoma have been connected to specific clonal gene arrangements. Chronic myelogenous leukemia has been shown by DNA probe use to be caused by a specific gene translocation. Although the use of probes for cancer may not be of value for production agriculture, pet owners will be interested in the accurate and specific diagnosing of neoplasms in dogs and cats. Of particular interest will be fast, simple and inexpensive kits for the detection of feline leukemia.

The area of quality control of biologics, both human and veterinary, always requires new tools to screen for and detect adventitious microorganisms in biologics. The sophisticated and very specific nucleic acid probes can detect certain microorganisms in cell cultures or production materials.

Performing diagnostic tests "on the spot" may appear as an idealistic goal, but needs to be considered. The technology for the ELISA can be brought into the field i.e., black boxes with monoclonal detection components can be operated in the back of a pick up truck. The original probe technology required the application of radioisotope techniques, but DNA probes can also be brought to the field using nonisotopic labels.

The sophisticated technology of nucleic acid hybridization enables the design of multiple detection probes in the one assay kit. These kits will enable the technician to determine the presence or absence of several infectious agents. The manufacturing of the multiple probes kit will be extremely cost effective in the livestock industry. DNA probe and ELISA kits are available for detecting residues, toxins, antibiotics and for determining pregnancy.

An effective application of the tools of biotechnology to problem solving in the animal health industry has been the marketing of a rapid DNA probe assay for paratuberculosis (Johne's Disease). Prior to the current assay a lengthily period of over three weeks was needed to provide a diagnose of suspected cattle. The first USDA licenced DNA probe kit for diagnosis of an animal disease is the available test for paratuberculosis in which the results can be obtained in an afternoon. A test for the rapid and accurate diagnosis of BSE is needed. Thus, the arena of animal health diagnostic lends itself to the application of nucleic acid probe technology and hybridoma technology.

2.4 Immunomodulation Products

Immunomodulators refer to materials that modulate or alter the immune responses. Obviously the immunomodulators of most interest are those that increase activity i.e., enhance or stimulate certain components of the immune response. Some immunomodulators also decrease activity (turn down specific functions) of certain of the immune responses. These compounds may be of value in providing anti-cancer or anti-inflammatory activity and are of use in human medicine.

2.4.1 Adjuvants. The use of specific immunogens in vaccine preparations provides for a specific targeting of the immune functions to protect against the disease. Non-specific (or nearly non-specific) material may be added to the vaccine preparations to increase the effect of providing protection against infectious disease. This is a type of immunomodulation, and the materials added are described as adjuvants.

In general adjuvants are added to vaccines because the desired effect of the designated protective immunogen in the preparation may not provide satisfactory protection without some enhancement. The immune responses to vaccines (protective immunogens) depend upon the physiological and nutritional state of the animal and are also variable from animal to animal. In most cases adding adjuvants "hypes-up" the activity of the immunogenic components in the vaccine and thus compensates for the variations and short comings of the immune response in the animal. In general these adjuvant type materials 1) enhance the effective specific immunogenic action of the vaccine components or 2) stimulate one or more areas of the immune response chain. Usually these immune stimulant activities are non-specific, but in some cases the respective material may have a primary effect on either the humoral (mainly B-cell activity) route or the cell mediated response (T-cell interactions).

The goals of desirable vaccines for animal health were previously examined. The goals of the development of adjuvants in animal health are similar: 1) the adjuvant needs to be easy to compound with the immunogen and to not alter the specific activity, 2) the materials should be non-toxic, and not yield residues in the meat of the animal. Historically some very tissue damaging adjuvants or adjuvant type materials have been administered to livestock and poultry. One of the important goals of an effective adjuvant is to not cause tissue damage, particularly, damage that will effect meat quality in the animal, and 3) the final point is not a surprise: these materials need to be inexpensive or "cost effective."

Some of the high tech areas of interest for adjuvant or immunomodulator research consist of developing specific simulators or enhancers of the T-cell or B-cell mediated functions. Materials that enhance the presentation of the specific antigenic epitope to specific immune cells (targets for phagocytic cells) in the host are of value in immunizing animals. Some adjuvants or carriers may act by strictly physical presentation mechanisms, while others act via specific receptor type interactions. Prime examples are the various liposome systems which have been shown to be very effective in targeting responses. The section on delivery systems also addresses the targeting of immunomodulators in animal health products.

2.4.2 Cytokines. The tools of genetic engineering and recombinant DNA procedures can be effective in the production of immune stimulants. The therapeutic application of biological response modifiers (BRM), or cytokines is another prominent R and D arena for immunomodulation products. Endogenous regulation of the immune system involves a series of complicated events, and cytokines is a generic term for the proteins involved in regulating the immune responses. Cytokines produced by lymphocytes are called lyphokines, when these biological response modifiers are produced by monocytes of macrophages they are referred to as monokines. Cytokines include 1) alpha, beta and gamma interferon, 2) interleukins (IL-1 to IL-12), 3) tumor necrosis factor, and 4) granulocyte-macrophage colony stimulating factor.

Advances in protein purification and DNA technology have made available supplies of recombinant human cytokines. Additionally cytokines have been molecularly cloned from economically important animals such as cattle and pigs. The availability of these recombinant cytokines has led to the investigation of their use for disease control in livestock. Cytokines inhibit a varying degree of species specificity. In food animals where cytokines have been compared in a homologous system, homologous cytokines are generally more effective.

The use of cytokines for immunotherapeutics appears to be of particular value in multiple infections. Control of these types of disease problems is extremely difficult and may be further complicated by additional factors of stress and nutritional deficiencies. Bovine respiratory disease complex is a striking example. Annual economic losses due to bovine respiratory disease complex range from $250 million to $1 billion. Several pathogenic agents are involved, e.g., viral organisms as well as bacterial organisms. The problems are particularly prevalent when cattle are stressed during movement; thus to the feed lot operators the problem may be referred to as "shipping fever." Injectable vaccines for control of respiratory infection are available and offer some success. Massive application of antibiotics can alleviate some of the loss. All applications require a cost/loss/death analysis by the contracting veterinarian. One method of decreasing the impact of this type of disease in cattle (and other food animals) is to increase the ability of the animal to withstand the infectious process by stimulating their immune systems with cytokines.

Additionally, cytokines have potential application to augment immune response in various periods during the production of farm animals when immune function may be low, such as the neonatal periods or pathogen-induced immunosuppression. Natural killer cell activity is very low in neonatal pigs, and it appears that cytokines, or cytokine-inducing therapies may be able to increase this host defense mechanism. Work in laboratory animals has demonstrated that cytokine-induced restoration of immune function is possible in animals that are immune compromised (immune deficient). Thus cytokine prophylaxis or therapy may be effective in domestic food animals for which stress or pathogen-induced immuno-suppression has been linked to disease susceptibility.

Cytokine therapy in human cancer patients continues to be an active area of research in tumor biology. Interleukins, tumor necrosis factor, and interferons are examples of cytokines used for stimulation of immune responses and regression of tumors in human patients. Most domestic food animals do not live long enough for tumors to present a serious health problem. In the arena of companion animals the situation is different. Presently the areas of viral infections leading to leukemia and anemia in cats are currently very significant points of research. Endogenous cytokines are used to modulate the immune response for the control of these cancers and tumor conditions in cats, dogs, horses, and other companion animals. The use of cytokine prophylaxis or therapy may become a cost effective procedure for prolonging the life and the quality of life in companion animals. The cost factor in using these cytokines becomes a focus of management. Management is the key item here.

Cytokines become one option in disease control. In actual practice the production specialist will consider the use of antibiotics, preventive vaccines and acceptable death factor in making management decisions on food animals in production settings. Note that cytokines normally will not present residue problem. In the dairy industry the additional decisions will include the labor component in therapy, the option of culling the cow and milk loss to residual antibiotic as a therapy treatment.

Delivery system options of the cytokines are important and these systems are described in section 5.

2.5 Genetic Manipulation of Animals for Disease Resistance

It was noted in the previous section that one method of combating losses to disease was to focus on the genetics of disease resistance in the host animal. There is a genetic component of susceptibility to virtually all animal diseases. This component can be modified in a number of ways. It is of course modified by natural selection. Secondly, it has been modified for years with selection (selective breeding). Because of recent developments it is now possible to enhance disease resistance in animals by recombinant DNA technology.

Various kinds of animal diseases can be addressed by genetic engineering. First there are the genetic diseases (such as anatomical deformities or metabolic deficiencies) usually defined as those that are due to a single gene and sometimes the absence or defect in a gene. These particular types of disease can lend themselves to genetic therapy. Gene therapy can be defined as the treatment of the animals who have genetic disease by transferring normal (other genes) into the defective diseased cell to correct the pathology caused by the mutant gene in the diseased animal.

The requirements that must be met before gene therapy can be accomplished are: 1) the gene must be identified, 2) the gene must be cloned, that is physically isolated by recombinant techniques, 3) a method must be developed to transfer the gene into diseased cells, 4) appropriate expression of the transferred gene in the target cell must be achieved and, 5) to be considered effective, gene therapy must be able to cure, arrest, or at least significantly improve the host animal. In general in this procedure the normal gene is only transferred to the somatic cells, the non sex cells of the body. Therefore, unlike transgenic animals, the new gene cannot be passed to offspring of a treated animal. This is of course the important technology that is being rapidly adopted in human medicine. The increasing knowledge of genetics and gene expression in all organisms will permit new strategies to be developed which will be applicable to gene therapy. Many of these new strategies will be developed by treating animals with genetic diseases and will be directly applicable to human patients.

One strategy is the systematic gene mapping of production animals, i.e., cattle and hogs. This project is underway as a result of funding source from federal agencies (USDA), academic institutions, and industry. When these gene maps are available the techniques of biotechnology will provide for strategic approaches to engineering animal resistance to a specific disease or to addressing overall disease resistance. One current method of choice for introducing genes into animals for gene therapy is the retroviral vector system. Retroviral vectors are used because they take advantage of certain properties of retrovirus which are useful for efficient, permanent gene transfer. By use of these retroviruses in poultry lines, an important disease resistance gene to Marek's Disease has been introduced into a chicken germ line.

Currently the tools of biotechnology play a role in the development of diagnostic nucleic acid probes linked to specific gene identification in farm animals. These procedures provide for the rapid and accurate genetic screening of large numbers of animals. Results from the screening can lead to breeding selection or in more sophisticated options pave the way for adding or deleting selected genes. In a wider use these procedures can be part of the development of transgenic animals. There are a number of sites in the immune components of the host which one could examine for genetic control of disease resistance. One site is the attachment of the pathogen, which involves receptors that are generally utilized by organisms to enter the cells. Certain examples of differences in receptors are known. There are swine that have specific *E. coli* receptors; and those that have modification of these receptors are more resistant to colibacillosis. Use of the specific DNA probes in conjunction with traditional breeding procedures can lead to control of colibacillis in swine herds.

Certain point mutations become identifiable only in mature or nearly mature animals. Usually these animals die or have to be destroyed, thus presenting economic losses in production herds. It would be efficient to identify the carriers of these mutations in the breeding stock and, of course, cull them from the herds.

An example is the implementing of an effective screening program for a point mutation which results in bovine leukocyte adhesion deficiency in Holstein dairy herds. DNA technology has led to the sophisticated targeting of the genetic defect. Diagnostic probes are available for rapidly detecting the carrier animals with this immune system defect. The organization of the dairy industry and availability of the diagnostic test developed to genotype cattle can lead to eradication of bovine leukocyte deficiency. These new procedures can be directly viewed as very cost effective in improving herd genetics.

In dairy operations new genetic approaches are always of interest in providing defense of the udder against mastitis infections. The pathogens which cause mastitis can be considered in two broad groups: contagious and environmental. The contagious pathogens are associated primarily with the udder and tend to be spread from cow to cow. The most common contagious pathogens are *S. aureus*, *Strep. agalactiae*, and *Strep. dysgalactiae*. Environmental pathogens are those present in the reproductive tract and the feces which in turn survive and multiply in the housing materials. These organisms are *E. coli*, *Strep. uberis* and *C. pyogenes*. Control of mastitis is a management point which involves good hygiene and proper dry cow therapies. These total regimens involve the use of vaccines, antibiotics and immunotherapeutics.

Another consideration is to achieve resistance to infection in the host cow. Two paths may be taken to achieve greater genetic resistance to mastitis: 1) select on the basis of resistance and 2) alter certain genes in the cow. *Staphylococcus aureus* is the organism causing the majority of infectious problems in mastitis. The anti-staphyloccal enzyme, lysostaphin, is an effective means of counter infections, and injection of lysostaphin into the mammary glands has shown protection against tissue damage caused by *S. aureus*. To control these infections in the udder one approach would be to produce transgenic cows with the genes to code for the production of lysostaphin which in turn would be secreted directly into the mammary glands.

2.6 Designer Drugs/Pharmaceuticals

Biotechnology has influenced the pharmaceutical industry primarily by facilitating the manufacturing of products (proteins) in heterologous cells. This is accomplished by introducing a segment of foreign DNA that encodes the desired protein under the control of the regulatory sequence of a host cell. This technology has led to vaccines, diagnostics, and immunomodulators as described in section 2.

The technology has now moved to the stage of "designer drugs." Other chapters of this monograph will discuss the details for the R and D for these pharamaceuticals.

The process of designing drugs is usually directed toward key enzymes. With the discovery and cloning of receptors these structures (receptors) have also become favorite targets. Receptors interact with signaling molecules (biomodulators) and hence provide a fundamental mechanism for regulating cell activity in response to the environment. An example is the case of polypeptide hormones which typically react with receptors that traverse the cell membrane. Binding of the hormone to the extracellular domain results in intracellular response which is specific for each receptor. The receptor is "turned on" by the ligand. Through genetic engineering, the extracellular regions can be produced in large quantities, independently of the rest of the molecule. These "domains" retain the same ligand-binding characteristics, hence they can be used efficiently to screen or select for molecules that bind like the natural molecules and act as agonists or antagonists. Hence, species can be developed that mimic hormones but have more favorable characteristics as do drugs. Usually the receptors are displayed in relatively low concentrations on the surface of cells, therefore the methods for developing agonists and antagonists are technically cumbersome. If one employs high concentrations of receptor domains, one can consider selecting the molecules that bind most tightly from among a large number of test molecules. This greatly facilitates the process of finding active compounds.

As expected, much of the research with animals is directed primarily to developing animal models for applications in evaluating drugs and biologicals in human medicine. However the direct role of developing such drugs for animal use is becoming more important. This is because the focus on the marketing of companion animal products can provide an important area for commercialization.

3. Research and Development Concepts for Production Enhancers

The use of biotechnology to aid in the efficient production of meat and animal products is well characterized and understood at the research and development level. For instance, the administration of bovine somatotropin (BST—sometimes referred to as bovine growth hormone) has for over 40 years been known to increase milk production in dairy cows. This BST can be derived "naturally" by extraction from the pituitary gland of cows or by the use of recombinant DNA technology. This latter source, often referred to as "synthetic," which is a misnomer, is derived after inserting the cow's natural gene into another organism e.g., a bacterium. By the use of fermentation, extraction and purification processes, it is possible to produce highly pure BST that can be administered daily to the animal to elicit the desired biological effect. Under many circumstances this protein not only increases the milk production of the animal (lbs/day), but can increase the duration of the lactation and increase the conversion efficiency of the feedstuffs to milk. All of this translates to a product that can cut the cost of milk production to the farmer. By maintaining his competitive edge, the farmer can maintain his profitability in the world market. While a number of companies are developing this market for commercialization world-wide, the product has not been approved by the FDA (U.S. regulatory body) at the time this chapter was written.

One of the powers of this technology is that the producer can increase the output of milk from the cow without altering the composition of the milk. A large number of studies have been performed that clearly demonstrate that the composition, nutrition and safety of the milk are not affected by this technology. In spite of this there appear to be opponents of the technology who simply ignore the scientific studies to promote their own agendas. Technically, this has been a success for the companies involved, although the overall commercial success of this project remains to be seen.

Another product in the meat arena is allied to BST and is the porcine equivalent. Porcine somatotropin (PST—sometimes referred to as porcine growth hormone), when administered to the growing hog, has three distinct but related effects. The first is that it increases the speed of growth (average daily gain). Thus the hog can get to market quicker. The second property is that the hog grows with a higher efficiency, i.e., it converts feed to lean meat more effectively (feed to gain ratio). Thus the producer will be presented with a feed bill that is lower per pound of lean (saleable) meat. The third property is that the hog does not put on as much fat in the latter stages of growth and stays leaner. This will result in a leaner animal, with less waste and a product that the consumer appears to prefer. The precise economic advantage of this can only be realized after the meat packer begins paying for the leaner carcass in reflection of the consumer's desire for a lean and, hopefully, healthier product.

All of these biological properties of PST are interrelated. It appears that PST acts to keep the metabolism of the hog in a more juvenile state, preventing it from entering the inefficient metabolic state associated with the final finishing stage. During these last few weeks, the animal increases its feed consumption and lays down considerable backfat during the time it is putting on the final muscle mass. PST acts somewhat like a natural partitioning agent and directs energy to lean muscle deposition and away from fat production, thereby improving the efficiency of feed conversion. While several companies are researching this product, none has been granted approval by the FDA at the time of writing. Again, these have been R&D successes and time will tell whether it will be a commercial success.

These two examples illustrate some of the concepts being investigated and pursued by relatively large commercial companies. It is very clear that there are potentially other applications for BST and PST. For instance, BST has been demonstrated (like PST) to improve the feed efficiency in beef cattle, which may lead to a new application for this compound. Similarly, PST might increase milk production to lactating sows which might influence the survivability for the offspring. These concepts are still in the R&D phase.

Of course a variety of other molecules and commercial targets are being pursued in addition. However, these examples serve to illustrate some of the key challenges that have been faced by companies in their commercialization programs.

4. Reproduction Technology

High technology advances are occurring in the field of animal reproduction. Research has shed new insight into the mechanisms controlling egg growth and maturation. Progress has also been made in understanding the control mechanisms that regulate the production of progesterone which is responsible for estrus cycle regulation. The new knowledge is aiding the development of precise methods of regulating the estrus cycle, inducing superovulation, and reducing heavy losses due to early embryo deaths that occur in all domestic animals.

Superovulation techniques enable the livestock manager to induce genetically superior cows to shed large numbers of eggs and to fertilize these eggs in vitro with sperm (which can now be sexed) from genetically superior bulls. The embryos can be split to produce multiple copies and transferred to recipient "surrogate" cows. The regulation of the estrus cycle is also needed to ready surrogate mothers to receive embryos. Embryo transfer provides for the improvement of livestock herds more rapidly than can be achieved with traditional breeding. Annually about 100,000 calves are born in the United States using embryo transfer techniques.

Early detection of pregnancy can enable the livestock manager to identify and rebreed animals that have not become pregnant. This has not been an easy task. Detection methods that are accurate, easy and inexpensive for these determinations are of interest. Several new methods utilizing recombinant products are under development.

The availability of techniques to pre-select the sex of the progeny hold great economic potential for livestock production. In the dairy industry females are the major income producers, while in the beef industry males are economically more valuable. Recent advances in the separation of X and Y sperm and the sexing of embryos have been achieved. These methods are now available to provide the degree of separation needed for commercial use.

5. Delivery Systems

The first round of products derived by biotechnology for animal agriculture have been protein in nature. Because proteins are, by and large, not orally active, or at least efficient, oral routes of administration have not been developed, they have to be administered parenterally to the target animal. This can be accomplished by administration intramuscularly, intraperitoneally or sub-cutaneously. In most cases, this is via a hypodermic needle and syringe. Furthermore, because target recombinant proteins are produced endogenously by the body, their turnover is rapid and their serum half life is short. In most cases, daily administration of the protein product is required to elicit the biological effect. While many products are being developed to be taken daily, many companies have recognized the desire to develop prolonged release systems. It should be recognized that second generation products with longer serum half-lives and delivery systems that allow absorption of these large molecular weight proteins are possible but this may require another 10 years to accomplish.

The disadvantages of the daily delivery system are many fold. With very tight economics on most of these biotechnology products, the extra cost of an injection per animal per day and the relative high labor costs have put severe economic constraints on product viability. Several companies have explored the possibility of using a single syringe for several animals or developing multidose delivery devices but all pose concerns with respect to the transmission of diseases. Furthermore, routine operations on most farms do not lend themselves to daily administration of products. When the typical dairy farmer brings the animals to the milking parlor twice daily (some are now doing it three and four times), this would not pose a major problem. However, in beef feedlots, the use of a BST type product to improve feed efficiency on a daily basis would pose special problems to assure each animal received its dose.

Prolonged release systems (PRS) offer many advantages over daily delivery systems. These PRS's decrease the labor costs to the farmer since the product has to be administered once every 2, 4, or even 8 weeks. Furthermore, operational systems on the farm are less disturbed. This would offer an advantage to a dairy farmer and especially to a beef feedlot operator. While the advantages appear very obvious there are several hurdles that have to be overcome by the developer of the product. The time and cost of developing a PRS are considerable and usually can only be finalized once the biologically active material and its manufacturing process have been delineated. While the variety of delivery systems is considerable, they all face similar problems.

The delivery system must deliver the activity to the tissues of the animal with the appropriate kinetics. This can be as a pulse (equivalent to a daily injection), zero order kinetics (continuous and constant) or first order kinetics (a pulse followed by decay). For this review, we do not intend to examine the merits of each system, since each molecule and the delivery profile should be determined empirically and then analytically. For all examples, several hurdles appear common. In all cases, biological compatibility is essential. The device or system can be recognized by the target animal as being foreign and during the course of the biological activity of the device, the body will attempt to encapsulate or inactivate the system. The success of this (from the animal's perspective) is dependent on the intended delivery span, the manner of administration or implantation, the material of construction, the integrity of the system and the animal body's ability to recognize foreignness.

A second challenge relates to the stability of the product. Being based on a protein, the product is relatively unstable, often requiring refrigerator temperatures prior to administration to the target animal. For a daily product, the protein is only exposed to adverse conditions after it has been injected and in general, it lasts but a few hours or a day at the most. However, prolonged release systems are implanted in the target animal at body temperatures which are ordinarily not recommended for routine product storage. In consequence, the development of delivery system must include a detailed study on the expected degradation pathway of the product under simulated body conditions. Any observed degradation under these conditions must be taken into consideration when the kinetics are determined. Proteins are very unstable in aqueous systems so PRS's that keep moisture away from the active agent have been the route that has resulted in the most efficient delivery systems.

Once an efficient PRS delivery system has been developed, it will be noticed that the efficiency of the system is often not as good as the daily. That is, it takes more activity per unit of time in the PRS delivery system versus a daily system to elicit the same biological response. This has a profound effect on the economics of the system.

6. Transgenic Animals

The use of biotechnology and genetic engineering to modify the genetics of animals has been researched over many years. It is considered to be the next step in the process of traditional animal breeding that mankind has been practicing for the last several thousands of years. Unlike traditional animal breeding where two animals, anticipated to contain desirable traits, are mated and the offspring screened for overall improvements, transgenic animals are considered to be the result of more directed, controlled and targeted breeding.

In the production of transgenic animals, a fertilized egg from a recipient animal (both parents are of good basic stock) is infected by a virus containing a desired gene, or alternatively, a gene cloned into a vector is injected into the egg. This transgenic egg is allowed to grow in vitro and then is inserted into a surrogate mother for development. The resulting offspring can then be bred to propagate the strain. Embryo splitting and in vitro fertilization are often used to speed the process. Once the animal stock has been established and its purity checked it is managed like any other highly valuable animal.

6.1 Transgenic Animals for Improved Productivity

In section 5, BST was discussed as a pharmaceutical to improve the efficiency of milk production and keep the cost of dairy products affordable to consumers. Clearly, administration of BST is the first step in the biotechnology agenda for improved agriculture. Besides the obvious second generation "BST" type approaches, there is the possibility of genetically modifying a cow so that she can synthesize more BST naturally, and produce more milk. Actually, we have been doing this for centuries in our traditional breeding programs to improve milk yields. Recently, with the help of improved analytical capabilities, we have demonstrated that higher producing cows make more BST than cows that are lower producers. However, it might be possible in the future to increase the copy number of BST genes or to implant a higher regulated promotor in front of the already present BST gene. With this, we would be able to encourage the cow to synthesize more BST and increase her milk production. However, the ability to insert the gene and control it appropriately has not been fine tuned.

6.2 Transgenic Animals for Improved Nutritional Composition

Similarly, the next generation PST type product would involve insertion of multiple copies of the PST gene or of more efficient promoters into the animal, thereby increasing the level of plasma PST. This should elicit the biological effect of interest, that is, leaner meat. Research to date has been encouraging, but the transgenic animal has not been able to assimilate the increased level of PST satisfactorily and has been reported to exhibit unusual adverse physiological effects. Clearly, we can get the gene expressed but perhaps not at the right concentration, in the correct location and for the necessary duration. While this research is exceedingly promising, we are perhaps 10 years away from commercial introduction of a major improvement by this route.

6.3 Pharm Animals

The use of farm animals to produce human pharmaceuticals has led to the use of the phrase "Pharm Animals." In this case livestock become the bioreactors to produce valuable pharmaceuticals that can be used to treat human diseases. Basically, the required gene is cloned into an animal, so that the product is produced and excreted into the animals' milk (thus preserving the animal for future production). This milk becomes the starting material (akin to a fermentation broth) for the purification process.

Over the years, the pharmaceutical industry has used animal products as pharmaceuticals for treating human disease. The obvious examples that come to mind are pork and beef insulin. In both cases, pancreases from abattoirs are harvested and become the material that is used in the downstream processing of the final pharmaceutical. However, the use of milk as a source of pharmaceutical and the use of transgenic animals pose special issues that the world regulatory agencies are wrestling with. Do we consider the animal like a fermentor with a product stream that is used downstream or do we consider these animals like blood donors in the development of plasma derived products? The former appears the more logical since these animals are kept under confined conditions with a tight control on their biology. Because this is a pioneer area, it could be considered as a high risk area in which to become involved.

At present the merits of using this as a manufacturing route are unknown. Until a product has been licenced and is for sale, it will be academic to determine the relative advantage of this route versus production from natural sources and from animal or bacterial cell culture. However, based on estimates of COGS, this could become a very attractive route to manufacture products.

7. Economic Targets/Marketing Forces

When developing a product for introduction into the food production industry, versus the human medicine or companion animal industry, many of the commercial assumptions or premises are radically different. The precise return to the food producer can be readily calculated. With this, severe restraints on cost of the product and the cost of manufacture are readily apparent. On the other hand, a cure for a fatal disease for a human has more latitude in pricing structure. Furthermore, the cost of cure for "Fluffy"—our companion cat—has more latitude than the price of a pound of ground round.

The example of BST in dairy cows serves to illustrate the point. From the research literature, it appears that the commercial dose of BST that will yield approximately 12 pounds of extra milk per day per cow is approximately 30-50 mg/day. This translates to about $1.20 per cow based on $12.00 per 100 pounds of milk. The USDA has estimated that the cost to the farmer could be between $.25 and $.75 per day, giving the farmer approximately a 2–4 times the return on his investment (it does take more feed to produce the milk). Thus the manufacturers will need to produce BST for between 1 and 2 cents per mg. Contrast this to the selling price for human somatotropin of greater than $10 per mg to treat hypo-pituitary dwarfism.

8. Food Products and Enzymes

Applying the tools of biotechnology offers the opportunity to custom design raw commodities with improved nutritional, functional, or processing characteristics that provide added value for the processor. Recombinant DNA technology can be used to construct microbial cultures for the production of fermented animal foods. These genetically engineered starter cultures can be utilized to improve the flavor, texture, nutritional quality, and digestibility of fermented dairy products. Customer demand for "natural" products has resulted in increased interest in microbially produced substances that can be designated as natural ingredients in foods.

Enzymes are used extensively by the food processing industry because they perform important functions in food systems. New enzymes with improved functionality for use in the food industry are of interest, and biotechnology can be used to provide new enzymes that function very effectively under the conditions required for food processing.

Products involved in food safety applications present another area of opportunity for commercialization of biotechnology products. DNA probes and monoclonal antibodies can be used to analyze raw materials and finished products for pathogenic organisms, as well as chemical and biological contamination.

These areas of R and D leading to genetically engineered products for applications in food processing are not the subject of this chapter. However, manufacturing and marketing opportunities exist in the area of value added processing of raw products derived from animals and new products derived by biotechnology are readily available.

9. Environmental Concerns in Livestock & Poultry Production

Livestock and poultry operations entail input and output material to the environment. Obviously large scale production facilities are not in highly populated areas, but because of the impact on the environment, the construction and operation of such facilities are subject to community regulated requirements (state and local laws) for environmental impact issues.

Treatment and removal of effluents and wastes from production operations become a significant cost. Confinement operations include treatment lagoons for effluents from hog and dairy operations. The goal is to use microbiological processing actions to neutralize offensive and toxic effluents before these are allowed to reenter the environment. State, local and federal statutes prevail over the allowance of amounts that enter streams and ground water. Most of the final wastes are not synthetic chemical compounds but are instead mainly biological degradation materials and end product metabolites. These are, of course, the very products that need to be kept from streams and water supplies.

Bioremediation is the biotransformation of pollutants, undesirable effluents, toxic substances and metals at the site in which they are found (*in situ*). Opportunities for commercialization of bioremediation products are discussed in another chapter of this monograph. Research ranges from understanding microbial communities to engineering *in situ* systems. The primary goal of research in bioremediation is the isolation, identification and biochemical characterization of microorganisms capable of carrying out specific chemical transformations. New and more effective microbes are always sought to improve the biological degradation of livestock and poultry effluents in lagoons. Genetic engineering of specific organisms for effective application of these treatment operations is needed.

An example of innovative research consists of the genetic engineering to reduce the amount of phytate (biodegradable substance found in grains fed to pigs and ruminants) that enters lagoons (run offs). Phytic acid is one of the major sources of phosphate needed for seedling metabolism (e.g., corn). Ruminants are able to efficiently metabolize the phosphate contained in grain. Monogastric animals (i.e., pigs and chickens), however do not necessarily fully utilize the phosphate contained in phytic acid. Although the major portion of this material is metabolized in the digestive process of the animals, significant phytate containing material winds up as effluent. Thus, research and development leading to enhancing digestion of this material via bioprocessing (microorganisms) have commercial value.

Alternatively the plant (crop) geneticists are employing genetic engineering procedures to develop plant seed/feed sources with lower amounts of phytate.

10. The Major Milestones in Commercialization

There are a multitude of strategies that a start-up company can use to become successful in the animal biotechnology industry. The precise one that will be the most successful will depend on a number of factors that are beyond the scope of this review. Several key questions should be addressed in the global long range business plan of the organization. Is the goal to be a long term “big” player in the animal business? Is the goal to be a “part” player (this will be discussed later)? Is the goal to develop an attractive company that will be acquired by a major corporation? Or perhaps, you recognize the need to start small but want to grow to become a big player. Are you developing products that impact the animal health industry, the food animal industry, human pharmaceuticals or companion animal industries? Irrespective of which of these are your targets and goals, several common steps must be taken in a timely fashion, which are often earlier than one might consider. Failure to address any or all of these steps in a timely fashion can lead to a very rocky road fraught with frustration and potential heartache.

The nine points to success are described below. These should be addressed and planned out early in the development process and should be run concurrently. The particular industry segment that you will be challenging, the types of product and the socio-political climate will determine the proportion of resources that are needed to be used to what end. In fact, some of the commercial potentials in the animal industry will not require heavy investment in some of these areas. However, astute business persons will be attentive to all these issues because they are dealing with a potentially rapidly evolving industry. It is important to remember that the best product (from a technical perspective) is not always the most commercially successful.

10.1 Business Strategies

It is critical to decide whether you plan to be a fully integrated animal industry player in the commercial field. This will require a complete infrastructure including R&D, Manufacturing, Regulatory Affairs, Marketing and Sales, PR and Communications. Clearly, this is a higher risk business but the potential gain is much higher. Many smaller companies choose a cooperative effort with a larger company because they recognize that their resources, both financial and personnel, are limited. In this case they focus on their strengths, namely R&D, and leave the other segments to the collaborator. Several companies such as Genentech have tried a range of approaches such as collaboration early, licensing technology to other companies prior to market entry of their new products.

Many companies often overestimate the value of their technology at the R&D stage. This is not because they do poor marketing estimates, but rather, they overestimate the probability of successfully introducing a product concept to market. It should be remembered that for every 10,000 compounds screened only one might become a product. Even those compounds that show promise in the initial screen have a small likelihood of commercial success (1 in 500).

Typically, many small biotechnology companies start out as small R&D boutiques led by or controlled by an academic. While the technology and the scientific challenges are well understood, the challenges of the business end are not usually his/her strength. It is critical to get good, objective business expertise early.

10.2 Technical Challenges

In addition to an understanding of the technology involved, one must have a detailed and realistic plan to move from the discovery mode into probe research, into a fully fledged commercial product. Milestones and goals must be clearly defined and then met for a successful product to enter market within the window of opportunity. This involves understanding the stability of the product, the dose of the compound, and the likely response and success rate in a realistic field situation. If we are dealing with a product to be administered to an animal, a product definition is critical with respect to prolonged release versus daily doses and the excipient with the compound. At these stages it is critical to determine the stability of the product and the storage conditions for the product.

With a clear definition of the product, usually manufactured at a small scale, a plan needs to be developed to adjust the product scale to that required to meet market size, market share and rate of market penetration. This is a two dimensional exercise because it requires both scale and timing for success. For those who have been involved in process scale-up, the task is recognized as the challenge it is. This exercise needs to be dovetailed in to the manufacturing components of the plan.

Overall, the cost of the R of R&D is enormous. This is a reflection of the intrinsic costs of the procedures and experiments and also the long time needed to execute a research program, both in personnel and infrastructure. The D of R&D is often less costly, relying on the expertise of persons outside the organization. This can considerably cut the costs (money and time) of the endeavor. Remember that the cloning exercise of biotechnology/genetic engineering is really development since the original discovery (R) of the molecule and its potential application has already been delineated. Some projects, with respect to cloning, do fall into the R aspect and take considerably longer to get to market.

10.3 Regulatory Hurdles

During the time that a product is being defined, it is essential to determine what impact government regulations will have on market entry. Some products of biotechnology might not require any interaction with any regulatory body. However, most do require a licensing or approval by at least one federal or state regulatory agency. Some products require a review and approval by more than one. Because this technology is very new, often it is not clear which ones are involved. Therefore to prevent any later difficulties, it is critical to develop a working relationship with all relevant agencies and determine what is required.

Once the appropriate agency has been determined, negotiation between the company and agency is critical to determine what information, data and studies need to be gathered and performed. Some of these studies can be very long, requiring several years to complete. Thus, a clear delineation of the scope and breadth of a study is critical. At the same time the forward thinking company will attempt to anticipate studies that will be required in the future. During the course of these studies and trials, a continuous dialogue with the agency is necessary to maintain a good working relationship.

Of all the aspects of product development and market introduction, the regulatory phase is perhaps the most frustrating because it is the one that appears to be the most out of the control of the interested parties. In addition, there is little harmonization of regulatory requirements between countries and studies that are acceptable in one country are rarely acceptable in another, even, and especially, in the technologically advanced countries like the United States, Japan and the EEC block. Products related to companion animals appear to be the area where the regulatory hurdles are most easily addressed. However, the areas of food animals do pose serious regulatory hurdles, because of the ever changing political and social scenes. An example would be the potential for a "fourth hurdle" in the EEC, where the social desire for the product would become a criterion for approvability. While this "fourth hurdle" was dismissed, it should be taken as signal for what might become imposed the future.

10.4 Commercial Potential & Competition

While you may believe that your product is the best thing since sliced bread, you must be attentive to the other products on the market or about to enter the market. In addition, what other technologies are behind you in the market race but represent the next generation product? Furthermore, how original have you been? Has another company or individual been developing a similar product? Will you protect your investment by a single patent, an array of patents or by trade secrets. In all cases, you have to assess your competition's ability to challenge your patents and your own ability to police your property rights. Continuous monitoring of your competition's progress is critical and must be integrated into your global business plan.

If you find that you have a well protected niche in a market, you need to determine what the overall potential of the market is. In this analysis, you can usually assess how much you can charge for your product, based on the expected response in the field, the value of the response, and the users' anticipated or needed return on investment. This analysis will assist you in determining how much your cost of goods (COGS) can be. This information must be integrated into the technical arena. This exercise should be done on a routine basis during the development phase of the product and into the commercial introduction and whenever new information could challenge previous assumptions.

10.5 Manufacturing and Quality Issues

Before embarking on designing and building a manufacturing plant, it is critical to determine in which countries you intend to sell your product. In most companies intending international marketing, the design is based on the most fastidious country, or that which will be the most fastidious over the life of the product. Retrofitting plants to meet future regulations can be costly.

Once the market scope is determined, the philosophy of plant operation needs to be delineated with respect to quality issues. Are you going to meet the required quality determined by the regulatory agencies or are you going to manufacture to a higher quality and use this strategy as a marketing tool after product entry? The philosophy of plant operation will, of course, be determined by whether you are using your own plant or using another company's operations as a toll manufacturer. The latter case is a more difficult challenge than the former, where philosophy can be built in from the start. However, the latter poses less risk financially than the former in a well written contract.

In either case, an assessment of the size or capacity needs to be determined especially with respect to timing. Less time is needed when you integrate your process into a preexisting plant operation than when you start from scratch in designing and constructing a plant. In all cases, application to the appropriate regulatory agency for an inspection is needed well ahead of commercial approval. Usually prior to the inspection, you need to have operated the plant to demonstrate an approvable process. This entails very costly operations and stockpiling of product prior to approval to sell the product.

10.6 Consumer and Retailer Education

This is an area that is critical for those technologies that impact the animal industry with respect to food production. However, it is not a major issue for products such as diagnostics, where the food does not come into intimate contact with the product, or with products for the companion animal industry.

Prior to commercial introduction of your product, you need to determine whether you intend selling food products derived from animals from your clinical trials. Clearly, you can cut the cost of the development phase of the product by doing this. However, you will be posed with certain challenges that are not inexpensive. If you determine that you wish to sell the food products, evaluate the public climate versus your technology. First determine the reaction of various anti-biotechnology activists and environmental and animal rights groups. Develop an educational strategy to inform the food industry well ahead. Remember that retailers can and will change their minds very easily. They need to know what the advantage for them is. Be prepared to address all issues that they raise and be prepared to take the issue or problem away from them. Remember that it is your problem and not theirs. They can do without your technology but you need their support.

These programs should continue well into the introduction of the product to the market, when the initial issues have either destroyed your product or the issues have become non-issues. Remember that a negative PR campaign that has begun fuels the media and it is difficult to step back from this attention without appearing to abandon your project. Even relatively small delays in approval can be very costly when you are headlines in the newspapers and lead story on TV.

10.7 Ethical Issues

It is critical to have very clear company philosophy on what products you will work on and what you will not work on. Do not simply evaluate your immediate area. The press and activist groups often make quantum leaps of logic that can be devastating for you if you have not looked into the future, the past and areas that are tangential to you. On several occasions, we have been challenged with press more interested in discussing Teenage Mutant Ninja Turtles (as examples of genetic engineering) than products that are saving lives. In the animal food industry some of the opponents will focus on animal rights (as food sources as well as for medical research) issues as well as environmental impact and family farm survival.

You must have a company spokesperson clearly delineated who has had training and experience in addressing press questions. Unfortunately a Ph.D. in molecular biology does not train a person to clearly communicate the facts of the area to the press. The image that is projected is often as important as the actual stance of the company.

10.8 Positioning Versus Activists

The name of the game is pro-active not reactive. It is critical to get out ahead of the game and develop people support for your technology. Look to the groups that you would trust for health and other key questions and do research to evaluate the credible sources. Be prepared to share with them the technology and the issues. Many of these groups are very pro-biotechnology in their own areas and need to know how your technology fits in with theirs. You will be surprised to see where allies can be found who are prepared to go that extra mile to help you. It is critical to develop allies based on common goals or at least common areas. This is an area that will take on even more proportions in the animal food arena whereas its impact in the companion animal industry should be minimal.

The small company can have a very difficult time with a well organized lobby. A very small activist organization such as Food and Water had a major impact on Vindicator (a gamma irradiation company in Florida) whose first market application was irradiation of strawberries to prevent spoilage. At time of writing, their attempts to enter the poultry business to prevent salmonella contamination of carcasses had not been successful.

10.9 Marketing to Meet Customers' Needs

Find out what the customer wants and needs and supply it. The first part of this, of course, must be done before the product even takes shape in the laboratory. Do not supply what you think he/she needs. Investigate governmental regulations for the future and plan to meet them ahead of the game. If your product is unique make sure that the customer knows the advantage of your system versus that of a perceived competitor. Remember that your customer may not be as turned on by high technology as you are. Demystify the technology to show that it is friendly and easy to use. If you are head to head with a competitor with a look alike product make sure you offer superior service, e.g., order taking system, delivery, problem solving, and technical service.

11. Summary

Applying the tools of biotechnology to animal biology has resulted in considerable research and development leading to many exciting products in the marketplace. However final commercial success of these potential products has been limited because products identified as biotechnology derived face more hurdles than those not identified as biotechnology derived. Major difficulties limiting commercialization include the expected, such as economics of production and regulatory approval, and the unexpected, consumer acceptance.

Diagnostic kits, which in essence contribute to improving the health of animals, present the best opportunities for commercialization. In particular, health products used on companion animals become ideal marketing areas.

Vaccines, immunomodulators or anti-infective products in general need to be cost effective for application in food animal production. While the cost of achieving regulatory approval may be significant for these anti-infectives, the important point is that it is difficult to bring to market a biotechnology product even though it is profitable and competitive. The most difficult biotechnology products to successfully commercialize are the ones that trigger the social activists as well as the consumer activists. These are situations where the public perceives genetic alteration or manipulation of the animal in unacceptable terms of risk/benefit—all risk and no benefit. Sound science and technology have yet to triumph over these faulty perceptions. The astute scientist and business person will have to recognize the need for addressing these perceived risks and involving consumers. The successful marketing and resulting profitability of these products remain in doubt.

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EXECUTIVE SUMMARY

Beginning with the Middle East oil crisis of 1973 and acerbated by the Persian Gulf crisis of 1991, many people in government, academia and industry became concerned about the strategic implications of a loss of a major source of crude oil for American industry. Accordingly over the following decade a large number of research programs were directed toward exploring the potential use of abundant renewable materials as basic feedstocks for fuels and chemicals.

Unfortunately, the softness in crude oil prices and, hence, chemical feedstock prices; the cultural attachment of the chemical industry to traditional synthetic chemical processes; and technoeconomic problems with the currently available bioprocesses diverted the attention of the management of large chemical companies from the biotechnology alternatives.

Nevertheless, opportunities for innovation exist for small research and development enterprises willing to take a mid-range view to the business potential for introducing new biotechnologies in this area. The objectives of this study are to identify strengths and weaknesses in a number or proposed bioprocesses and to assist in developing an ongoing research strategy along economically relevant lines.

Synthetic Petrochemical Markets

To assist in developing a plan for relieving the threat of disruption of foreign oil to the American chemical industry, an analysis was made of the feedstock origins and alternatives for manufacturing the specialty and commodity chemicals that make up the U.S. "synthetic organic chemicals" industry. The industry comprises a large number of products. About 390 of these are produced at over one million pounds per year. These products collectively amount to 316 billion pounds valued at over $110 billion.

Specialty chemicals, as the name implies, are low volume (below 100 million pounds per year) but high value (over $1.00 per pound) products that usually evolve from a proprietary product or process patent position held by a single or a limited number of manufacturers.

Commodity chemicals—those produced at over 100 million pounds per year—account for about half of the total number of chemicals but control 98% of total production and 96% of total value. The five major feedstocks: ethylene, propylene, benzene, toluene and xylene form the nucleus. With their single derivatives they account for 169 billion pounds or 53% of all chemicals.

The Biomass Alternative

The production of chemicals from renewable domestic materials can be considered as an alternative to continued dependence on an uncertain foreign supply of fossil feedstocks. In this section the generic "business of biomass" was explored from the point of view of the six factors that must be controlled in any successful business: market potential, marketing position, product position, raw material supply, process position, and competitive cost advantage.

About 93% of the total production of the industry, or 294 billion pounds valued at over $100 billion, could be derived from renewable resources such as corn starch and lignocellulose in the form of wood chips or agricultural residues. This amount exceeds the personal purchase of automobiles in the Unites States and is 6.5% of the gross national product for goods and 2.5% of the total GNP.

In regard to marketing and product position, small startup companies would be advised to seek to develop specialty chemical products for in-house exploitation or to team up with a larger, established chemical company for developing new routes to commodity chemicals.

One of the most important aspects of a commodity chemicals business is that of raw material position. There are two basic renewable feedstocks in nature of interest here: starch and lignocellulose. In practical economics, starch in the United States refers almost exclusively to corn starch, the supply of which is controlled by the wet process corn industry. Lignocellulose refers mainly to wood chips, presumably available now through the infrastructure of the forest products industry, and, potentially, to corn stover, cereal straw, or municipal solid wastes. Excluding the olefins: ethylene and butadiene, the entire U.S. supply of 13 major oxychemical feedstocks could be produced from only 11% of the annual U.S.

corn supply of 7.4 billion bushels. This amount is about the amount of corn that corn refiners presently use annually. Likewise it would only take about 3% of the available annual excess cellulose supply of 770 million dry tons (net of forest mortality and removals) to do the same job. Clearly, there is an ample raw material supply available for all specialties and at least the major commodity products, provided that a business system can be developed to get the biomass to the right place at the right price.

Only four generic processes are needed to produce all the almost 300 billion pounds of chemicals potentially amenable to a biomass origin: fermentation, hydrogenolysis, gasification, and hydrogenation. These processes are already technically demonstrated at least at pilot scale. Fermentation could be used to produce oxychemicals, such as ethanol, acetic acid, acetone, butanol, glycerol, citric acid, fumaric acid, etc. Hydrogenolysis could be used to produce sorbitol, as is presently the case, or potentially other polyhydric alcohols such as ethylene glycol. The hydrogenation of lignin/cellulose residues, in a manner similar to the hydrogenation of coal, has already been well explored as a route to phenols and other aromatics. Finally, gasification of biomass could be used to provide the synthesis gas (hydrogen and carbon monoxide) needed for this and other transformations.

Under the biomass scenario, ethylene and propylene would be produced by dehydration of the respective alcohols. Ethanol would also become the source of butadiene (as it was during World War II). As a result, ethanol could become the ranking feedstock. Its derivatives could account for a third of all organic chemicals; while propanol derivatives could account for another 10%.

Competitive prospects for biomass commodity chemicals are currently unfavorable as a result of: (1) generic deficiencies in fermentation processes with respect to generally low (below 5%) product concentrations and slow fermentation rates, and (2) lack of a present competitive advantage for renewable materials compared with depressed prices for crude oil. However, research can alter the first limitation and Middle East politics, the second.

In the meantime, the continuation of a national research program on biomass conversion is strongly urged as a strategic insurance policy to protect the American organic chemicals industry against further disruptions in crude oil-based feedstocks.

Recombinant Aerobes

Productivity of aerobic fermentations is often limited by the rate at which cells can aerobically catabolize the carbon source. Oxygen limitations frequently result in generation of growth-limiting metabolites. All approaches thus far have been concentrated on improving oxygen mass transfer rates by mechanical means. In contrast, a recent discovery has shown that insertion of hemoglobin into *E. coli* by genetic engineering accelerates cell growth and increases final cell density.

Stimulated by this innovation, this study appraised the technoeconomic potential for improved fermentations based on recombinant aerobes that grow faster and to considerably greater cell densities and with higher product concentrations than conventional cells. Possible reductions in fermentation cost for four specialty products based on this genetic approach were determined. It was concluded that so far as fermentation economics are concerned research in this area should focus primarily on means for reducing process investment

Ethanol

Ethanol appears to be a key factor in the "biomass alternative" to fossil feedstocks for producing fuels and chemicals. If produced at a low enough price relative to crude oil, it and its derivatives could account for 159 billion pounds, or 50%, of the U.S. production of synthetic organic chemicals, presently valued at $113 billion. This use would consume 4.2 billion bushels, or about 54%, of the corn crop.

A 1970's batch fermentation plant operating with *Saccharomyces* cerevisiae, if built a decade later, would have to sell product at $2.58 per gallon and could not compete with ethylene-based synthetic ethanol plants. This poor competitive position results from a 73% increase in construction cost between an old 1976 plant and a new 1986 plant.

This study evaluated the potential savings in ethanol manufacture to be gained by applying advanced process engineering or genetic engineering of improved organisms, centering on the use of fluidized bed bioreactors containing immobilized cells of either the yeast or the bacterium: *Zymomonas mobilis*. These fermenters can operate at high cell densities by either containing the immobilized cells or by recycling after separating them from the beer.

An existing plant, retrofitted to the advanced technology, but operating in a batch mode, could produce at about $1.69 per gallon based on $0.065 per pound sugar.

A new continuous plant could produce at about $1.82 per gallon based on *Zymomonas* or $1.97 per gallon based on the *Saccharomyces* yeast. The bacterium has a competitive edge as a result of its lower sensitivity to product inhibition.

There appears to be no inherent design limitation to effect the engineering improvements required for the advanced process. In a longer-term, more difficult research effort, it might be possible to reduce or eliminate product inhibition to reduce cost even further.

Acetic Acid

In this technoeconomic evaluation of the manufacture of acetic acid by fermentation, the use of the bacterium: *Acetobacter suboxydans* from the old vinegar process was compared with expected performance of the newer *Clostridium thermoaceticum* bacterium. Both systems were projected to operate as immobilized cells in a continuous, fluidized bed bioreactor, using solvent extraction to recover the product.

Acetobacter metabolizes ethanol aerobically to produce acid at 100 g/l in a low pH medium. This ensures that the product is in the form of a concentrated extractable free acid rather than as an unextractable salt. Unfortunately, yields from glucose by way of the ethanol fermentation are poor but near the biological limits of the organisms involved.

Conversely, *C. thermoaceticum* is a thermophilic anaerobe that operates at high fermentation rates on glucose at neutral pH to produce acetate salts directly in substantially quantitative yields. However, it is severely inhibited by product, which restricts concentration to a dilute 20 g/l.

An improved Acetobacter system operating with recycled cells at 50 g/l appears capable of producing acid at $0.38/lb, as compared with a $0.29/lb price for synthetic acid. However, this system has only a limited margin for process improvement.

The present *Clostridium* system cannot compete since the required selling price would be $0.42/lb. However, if the organism could be adapted to tolerate higher product concentrations at acid pH, selling price could be reduced to $0.22/lb, or about 80% of the price of synthetic acid.

ABE Solvents (Acetone, Butanol and Ethanol)

Product concentrations in the old Weizmann fermentation process for producing butanol from corn were limited to at most 10-15 g/l as a result of a severe feedback inhibition of the organism. Consequently the process could not compete economically with the newer synthetic processes.

More recent fermentation programs have been aimed at using suitable solvents to remove the product from the aqueous fermentation medium as fast as it forms, thereby circumventing the inhibition problem. Thus, the new extractive fermentation approach would represent a major breakthrough in not only the Weizmann system, but generically any fermentation process that suffers from product inhibition.

In this section, the design, performance, and projected economics of a new process now being developed for the in situ, single-stage, solvent extraction of products within a multiphase, fluidized bed bioreactor are compared with those for an extractive fermentation process in which the beer is continuously treated in an external multistage extractor before recycling back to the fermenter.

If research goals are met, product selling prices for either process in the range of $0.35-$0.40/lb would be competitive with those for synthetic butanol.

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Chemicals from Renewable Natural Resources

A Technoeconomic Guide to Research and Commercialization of this Area of Biotechnology

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Key words: acetic acid; acetone; bovine growth hormone; butanol; chemicals; citric acid; enthanol; fermentation; lignocellulose; monosodium glutamate; renewable resources; technoeconomics.

PART I

Introduction

Beginning with the Middle East oil crisis of 1973 and acerbated by the Persian Gulf crisis of 1991, many people in government, academia and industry became concerned about the strategic implications of a loss of a major source of crude oil for American industry. Accordingly, over the past decade a large number of research programs have been directed toward exploring the potential use of abundant renewable materials as basic feedstocks for fuels and chemicals.

Unfortunately, the softness in crude oil prices and, hence, chemical feedstock prices over the past decade; the cultural attachment of the chemical industry to traditional synthetic chemical processes; and technoeconomic problems with the currently available bioprocesses diverted the attention of large chemical companies from the biotechnology alternatives.

Nevertheless, opportunities for innovation exist for small research and development enterprises willing to take a mid-range view to the business potential for introducing new biotechnologies in this area.

This chapter provides a generic overview of the potential for biomass-based chemicals and evaluates the technical and economic status of several newly conceptualized processes for producing aerobically produced specialty chemicals, and the important commodity chemicals: ethanol, acetic acid, butanol and acetone, which are possible candidates for research support. The objectives of the project are to identify strengths and weaknesses in the proposed processes and to assist in developing an ongoing research strategy along economically relevant lines.

1. Product Potential

The products that were studied presently comprise a collective U.S. market for 10.7 billion pounds valued at $2.8 billion. If their manufacturing processes were converted from petroleum feedstocks to corn they would consume 556 million bushels. Furthermore, if ethanol could be produced at a low enough price to serve as the precursor to ethylene and butadiene, it and its derivatives could account for 159 billion pounds, or 50% of the U.S. production of 316 billion pounds of synthetic organic chemicals, presently valued at $113 billion [1]. This use would consume 3.4 billion bushels or about 45% of the corn crop. In addition, the use of butanol for diesel blends or in jet fuel blends to enhance the range of military aircraft could increase further its market.

2. Bioprocess Problems

At the present state of the antiquated art for producing these products from corn by fermentation, product costs do not appear competitive compared with prices for incumbent petroleum-based chemicals. Industrial interest in fermentation chemicals had revived in the 1970's as a result of the oil crisis. However the subsequent softening in oil prices in the 1980's removed the competitive edge of renewable materials compared with fossil feedstocks and resulted in an almost complete loss of momentum in research in this area of biotechnology.

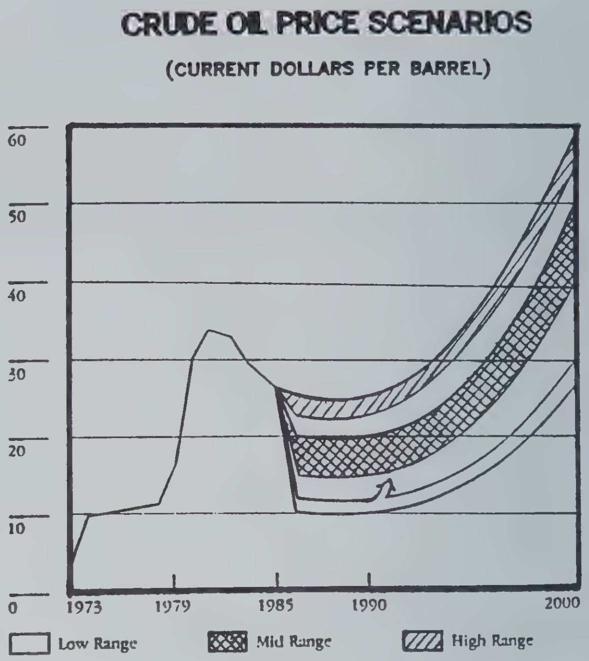
In general, fermentation processes have two major problems:

(1) Inherently poor yields resulting from the production of by-products, including high levels of carbon dioxide and hydrogen needed to maintain the electronic balance of the metabolism of the organism, coupled with the current relatively high cost of renewable sugars and starches compared with the presently depressed prices for petroleum.

(2) The inhibition of most organisms by their own products, which causes the fermentation to shut down after reaching only low, ca. 1%, product concentrations; as a result of which the recovery of product from dilute aqueous solution is accordingly expensive.

The raw material cost problem will presumably rectify itself in a few years after increased demand for oil relative to Middle East production capacity and further Middle East turmoil again force oil prices to rise. Conoco predicts that this will happen in the 1990's (fig. 2), at which time it is expected that the United States will be importing half of its oil supply instead of the 7% it imported at the time of the 1973 oil crisis [2].

One possible solution to the inhibition problem would be to apply extraction or distillation as an integral part of the fermentation process so as to remove the product from the field of fermentation as rapidly as it forms. In the case of an external multistage extraction process this is expected to permit a proportionate increase in cell density while maintaining product concentration in the fermenter near the threshold of inhibition. As a result, volumetric productivity increases and fermenter investment and cost decrease. Alternatively, in the case of an in situ single stage fermenter/extractor, this is expected to increase productivity and effective product concentration while maintaining low concentrations in the beer.



CONOCO, INC.

Figure 2

3. Outline of the Report

This chapter consists of seven sections:

Part I. *Introduction*. Which introduces the objectives of the study, the business potential, the technoeconomic problems now facing the introduction of the alternative biotechnology, and suggestions for generic research directions that appear to have economic significance.

Part II. *The Synthetic Petrochemicals Markets*. Which outlines the nature of the organic chemicals industry and the makeup of its products.

Part III. *The Biomass Alternative*. Which converts, in theory at least, the organic chemicals industry from a petroleum base to a biomass base and identifies the most important of the bio-based products. This section also considers generically a new business in bio-based chemicals from the point of view of each of the elements making up a good business: market potential, marketing position, product position, raw material position, and competitive cost advantage.

Part IV. *Specialty Chemicals via Recombinant Aerobes*. Which appraises a new approach to producing bovine growth hormone, a functional cloned protein, glutamic acid and monosodium glutamate, and citric acid. The approach is related to developing aerobic organisms that are better able to transfer oxygen in a dense, oxygen starved medium and can be applied to many other specialty product ventures.

Part V. *Ethanol*. Which appraises new processes for producing fermentation-grade ethanol having a competitive advantage over incumbent 1970's plants.

Part VI. *Acetic Acid*. Which compares the potential for a new one step process with that of the older two-step "vinegar" process.

Part VII. *Acetone/Butanol/Ethanol*. Which identifies problems with the old Weizmann ABE process and develops an alternative process development scenario to reduce costs.

PART II

Synthetic Petrochemicals Markets

1. The Database

Statistics on the production and sales of synthetic organic chemicals are compiled annually by the United States International Trade Commission. This study relied heavily on 1985 data from this source [1] supplemented by information from the Chemical Marketing Reporter [2] and the Modern Plastics Encyclopaedia [3] and estimates by Bio En-Gene-Er Associates, Inc.(BEA) in compiling its database. The database was limited as a practical matter to products produced at annual rates over one million pounds.

The database that was developed contains information on production volume and value, sales volume and value, and the feedstock origin of and intermediates for each chemical. The sales data do not reflect the value of captive intermediates included in the production data. Also by no means does the database include all organic chemicals produced in the United States. There are a number of reasons for this:

(1) As noted, the study was limited to production levels over one million pounds. However, the aggregate amount of products produced at lesser volumes is estimated to be only a few percent of the production listed in the database.

(2) Government statistics include only those compounds reported to be involved in commerce. As a result, many captive intermediates, such as adiponitrile and hexamethylenediamine which are important precursors to nylon, are not included. For the same reason, the sales volume cited in the database are generally smaller than production volume as a result of captive use. As an example of this, ethylene dichloride, one of the most important of the ethylene derivatives, is produced at a rate of 12 billion annual pounds, but sales only amount to about 400 million pounds—the rest is used captively.

(3) The government database refers to "synthetic" organic chemicals and, hence, ignores many other types of product. Nevertheless, the purposes of this study are still served since the emphasis here is on replacing synthetic petrochemicals by biomass-based chemicals.

It should also be noted that the data are not mutually exclusive in that many compounds on the list are intermediates for others on the list, i.e., ethylene to ethylene oxide to ethylene glycol to 2-ethoxyethanol, etc. Hence, the aggregate sum of all chemicals relates to a flow of materials and value through the industry rather that a sum of feedstock needs.

2. Overall Position

About 390 organic chemicals were identified having production levels above one million annual pounds. These products comprised 316-billion pounds valued at the manufacturers level of over $110 billion in 1985. (Table 7) This amounts to a weight average value of $0.35 per pound. As can be seen in figure 3, the average is heavily skewed to the high volume chemicals.

Of the 390 chemicals, the top five, which had production levels over 10-billion pounds each, accounted for 25% of production and 9% of value. Similarly the top 19 each exceeded 5-billion pounds and accounted for 55% of total production and 30% of value.

Over half of the products had production levels over 100 million pounds and accounted for 98% of total production and 96 % of total value. Hence, from the standpoint of relevance to the *national*

Table 7

SYNTHETIC ORGANIC CHEMICALS
1985 U.S. PRODUCTION

PRODUCTION LEVEL MILLION PPY	NO. OF PRODUCTS	TOTAL PRODUCTION		TOTAL VALUE	
		MM PPY	%	$MILLION	%
OVER 10,000	5	78,276	24.8	$10,070	8.9
5,000-10,000	14	94,650	30.0	24,164	21.4
1,000-5,000	40	82,623	26.1	36,733	32.5
500-1,000	43	29,557	9.4	17,106	15.1
250-500	48	17,719	5.6	13,282	11.8
100-250	53	8,315	2.6	6,757	6.0
SUBTOTAL	203	311,140	98.5	108,113	95.7
50-100	38	2,643	0.8	1,905	1.7
10-50	79	1,895	0.6	2,112	1.9
1-10	70	290	0.1	815	0.7
TOTAL	390	315,968	100.0	$112,946	100.0

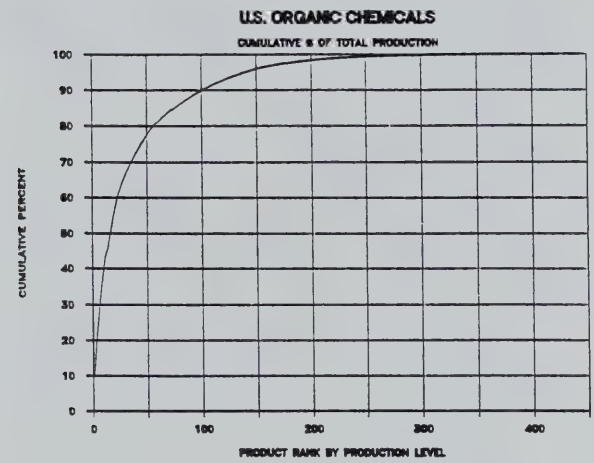


Figure 3

economy, government supported research programs should be directed toward these high volume commodity chemicals. On the other hand, the research efforts of small startup companies may be better directed toward developing those expensive specialty chemicals of current interest to industry.

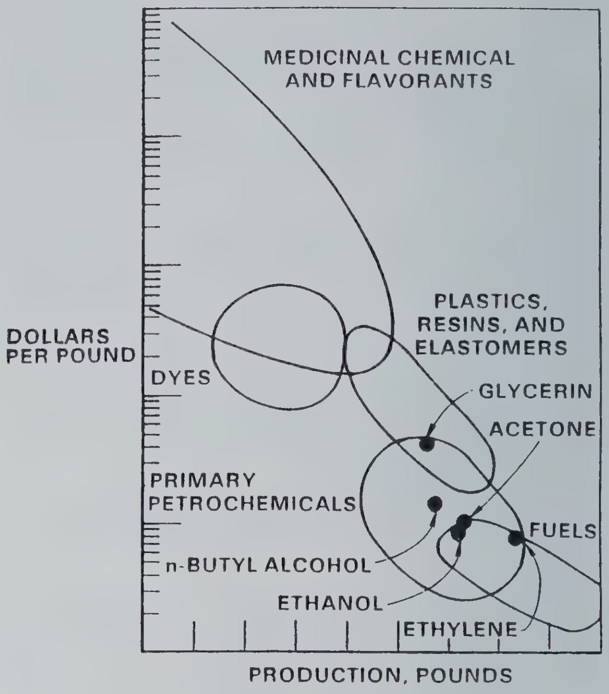


Figure 4

3. Price/Volume Relationship

Within product classes, price decreases as production volume increases. Generally, as shown in figure 4, products like medicinal chemicals, fragrances and flavors lie at the high value/low volume end of the scale [4]. Plastic resins and elastomers are in the middle of the volume spread and priced above the primary petrochemicals from which they are made. Fuels are on the bottom of the value spectrum.

Price/volume data from the database lie on a broad band as a result of the mixing of various industrial classes. A better picture of the average price/volume relation can be obtained from the normalized data of figure 5. At present, commodity chemicals are priced under $1.00 per pound.

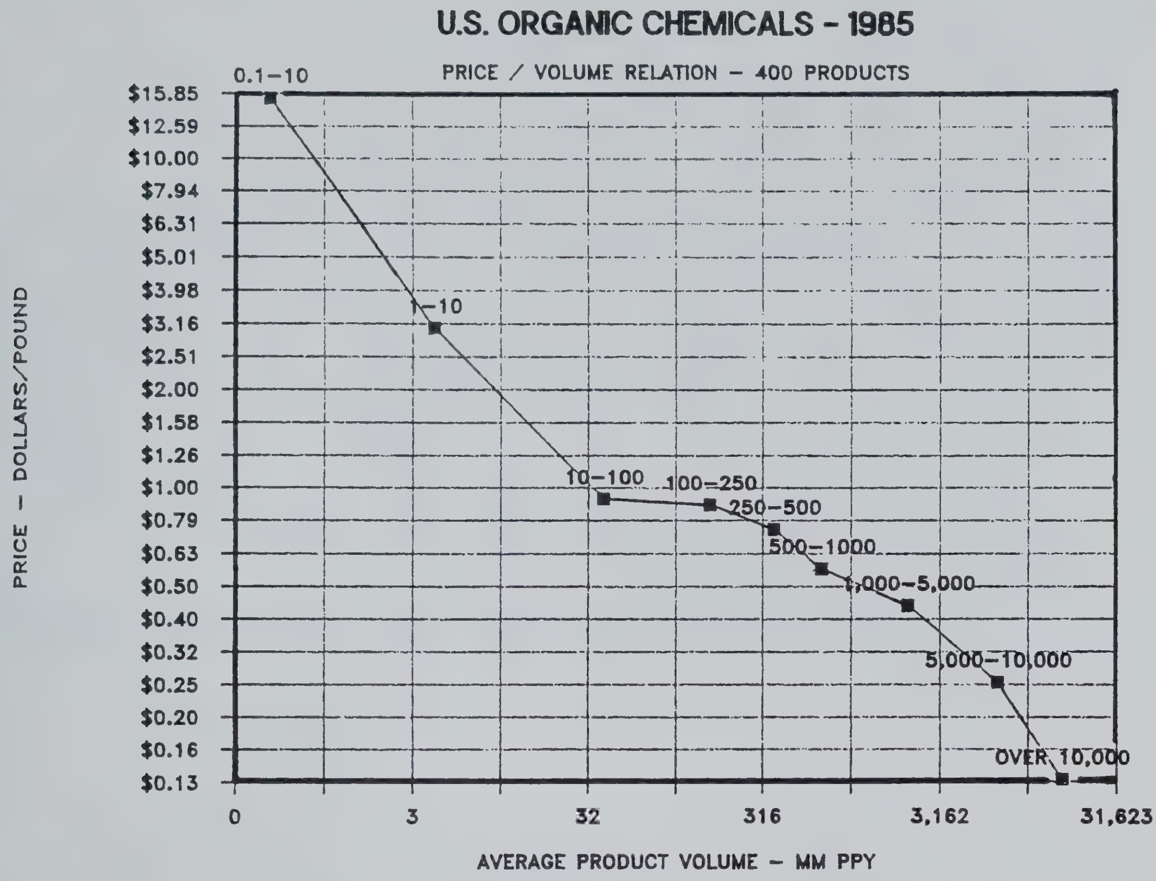


Figure 5

4. Primary Feedstocks and Derivatives

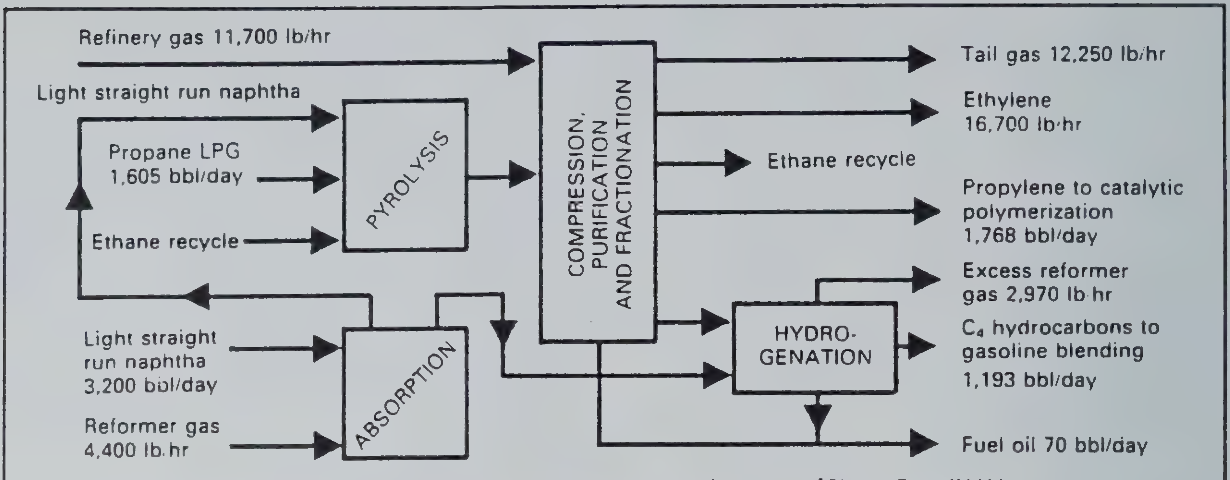
In order to structure the relationship of intermediates, each compound was appraised as to the presently preferred method of manufacture, using standard texts on the subject [5-7] plus the collective experience of the BEA staff. The immediate intermediates used to make each compound were identified and followed down the synthesis chain to the original "primary" feedstock. Primary feedstocks are defined here as those materials first identified by name out of the petroleum mix in the refinery. Ethylene and propylene are examples. The manufacture of these feedstocks from refinery gases is shown in figure 6 [8].

The data for all products were sorted by primary feedstock to show the derivatives from each feedstock and the combinations of feedstocks used. These results are summarized in Table 8, which categorizes production as to whether it refers to a primary feedstock, a derivative of a single primary or a derivative of a combination of primaries.

Out of 316-billion pounds of synthetic organic chemicals, 96-billion or 30% is represented by the primary feedstocks; 140-billion or 44% by the derivatives of single primaries; and 79-billion pounds by derivatives of combinations of primary feedstocks.

It is interesting to note that the big five: the olefins, ethylene and propylene, and aromatics, benzene, toluene, and xylene (BTX) comprise 69-billion pounds or 72% of all primary feedstocks, while these and their single derivatives account for 169-billion pounds or 53% of all chemicals. In addition these strategic feedstocks are also involved in additional combinations (Table 9). (* Please note, however, that the total for combinations is not additive because of duplications within derivative combinations).

Therefore, any plan for relieving the pressure of foreign oil must take into account the alternatives to these feedstocks, particularly ethylene (fig. 7).


Refinery gas 11,700 lb/hr
Light straight run naphtha
Propane LPG
1,605 bbl/day
Ethane recycle
PYROLYSIS
COMPRESSION, PURIFICATION AND FRACTIONATION
Tail gas 12,250 lb/hr
Ethylene
16,700 lb/hr
Ethane recycle
Propylene to catalytic polymerization
1,768 bbl/day
Excess reformer gas 2,970 lb/hr
HYDRO-GENATION
C_4 hydrocarbons to gasoline blending
1,193 bbl/day
Light straight run naphtha
3,200 bbl/day
ABSORPTION
Reformer gas
4,400 lb/hr
Fuel oil 70 bbl/day

Flowchart for ethylene and propylene production from refinery gas, [Chem. Eng. (N.Y.), Sept. 1, 1961 and M.W. Kellogg Co. see detailed flowcharts and data in Kellograms No. 1 (1962) and No. 1, 1961]

Figure 6. A schematic showing the manufacture of ethylene and propylene from refinery gases.

Table 8

MAJOR ORGANIC CHEMICALS
1985 U.S. PRODUCTION
(MILLION POUNDS)

	PRIMARY FEEDSTOCK	----DERIVATIVES---- SINGLE FEEDSTOCK	FEEDSTOCK COMBO´S
ETHYLENE	29,847	76,703	64,181
PROPYLENE	14,887	17,989	43,133
BUTADIENE & BUTENES	3,698	1,396	16,252
SUBTOTAL	48,431	96,087	123,566
XYLENES, m,o,p	9,918	2,304	21,324
BENZENE	9,390	2,569	60,589
TOLUENE	5,074	230	5,017
CYCLOHEXANE	1,657	3,554	2,246
SUBTOTAL BTXC	26,038	8,657	89,175
	0		
CH4/SYNTHESIS GAS	0	26,989	36,432
NATURAL PRODUCTS	0	8,401	4,420
TOTAL	74,470	140,135	79,831 *
	0		
ETHANE	5,631		
PROPANE	10,305		
n-BUTANE	2,214		
ISOBUTANE	1,639		
n-PENTANE	107		
HEXANE	482		
n-HEPTANE	124		
SUBTOTAL	20,503		
	0		
PENTENES	973		
DICYCLOPENTADIENE	64		
GRAND TOTAL	96,010		

* Column does not add because of duplications within derivative combinations.

Table 9

In Million Pounds

	Primary Feedstock	Derivatives Single	Combinations
Ethylene	29,847	76,703	64,181
Propylene	14,887	17,989	43,133
Xylenes	9,918	2,304	21,324
Benzene	9,390	2,569	60,589
Toluene	5,074	230	5,017
Total	**69,116**	**99,795**	**47,065***

*Column does not add because of duplications within derivative combinations

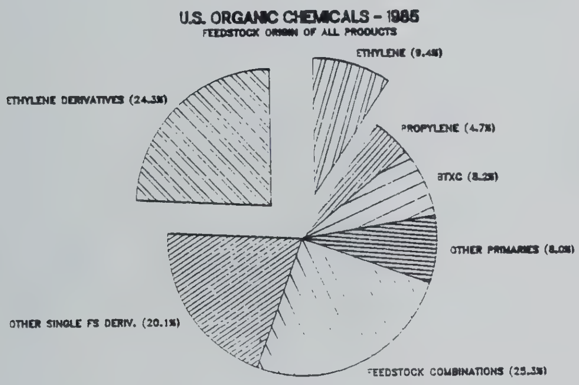


Figure 7

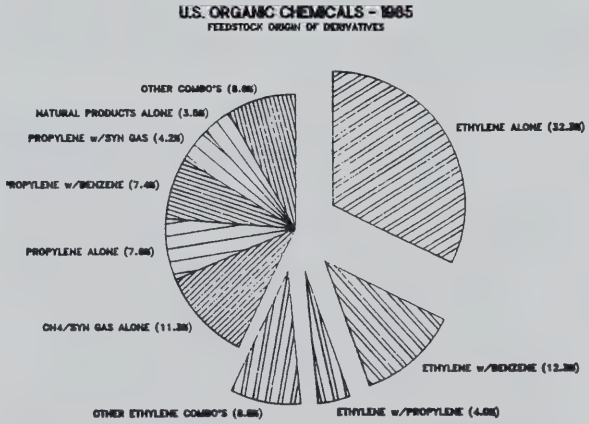


Figure 8

5. Primary Feedstock Combinations

In assessing the importance of feedstocks to the national chemical economy it is also important to recognize the interaction of feedstocks in producing derivatives in addition to the importance of the feedstock alone. These data are summarized in figure 7. Figure 8 is expanded in Table 10 to show the combinations of the various feeds. Considering the origin of derivatives, the importance of ethylene is overwhelming. Out of a total derivative pool of 220 billion pounds, derivatives of ethylene alone account for one-third. Combinations of ethylene with benzene, propylene, synthesis gas or butadiene also rank highly.

Derivatives of propylene alone or in combination with benzene, synthesis gas or ethylene are second to ethylene derivatives in volume. Although a case can be made for concentrating research on a single feedstock, such as ethylene, it is also important to recognize the need for a broader feedstock mix in order to reach a balance of products for the overall economy.

Table 10

INTER-RELATION AMONG MAJOR FEEDSTOCKS

(MILLION POUNDS PER YEAR - 1985)

	PRIMARY	DERIVATIVES WITH OTHER FEEDSTOCKS									
	FEEDSTOCK	ETHYLENE	PROPYLENE	BUTA+	XYLENE	BENZENE	TOLUENE	CYANE	CH4/SG	NATURAL	TOTAL
ETHYLENE	29,847	76,703	9,434	5,178	7,703	29,204	2,900	0	8,056	1,706	140,884
PROPYLENE	14,887	9,434	17,989	1,471	2,268	17,708	1,481	37	9,970	764	61,122
BUTADIENE & BUTENES+	3,698	5,178	1,471	1,396	0	5,177	8	2,172	2,246	0	17,648
SUBTOTAL	48,431	91,315	28,895	8,044	9,971	52,089	4,388	2,209	20,273	2,470	
XYLENES, m,o,p*	9,918	7,703	2,268	0	2,304	1,394	0	0	8,203	1,756	23,628
BENZENE	9,390	29,204	17,708	5,177	1,394	2,569	0	0	7,102	4	63,157
TOLUENE	5,074	2,900	1,481	8	0	0	230	0	628	0	5,247
CYCLOHEXANE**	1,657	0	37	2,172	0	0	0	3,554	37	0	5,800
SUBTOTAL BTXC	26,038	39,807	21,493	7,357	3,698	3,963	230	3,554	15,970	1,760	
CH4/SYNTHESIS GAS		8,056	9,970	2,246	8,203	7,102	628	37	26,989	190	63,421
NATURAL PRODUCTS		1,706	764	0	1,756	4	0	0	190	8,401	12,822
TOTAL	74,470	140,884	61,122	17,648	23,628	63,157	5,247	5,800	63,421	12,822	
ETHANE	5,631										
PROPANE	10,305										
n-BUTANE	2,214										
ISOBUTANE	1,639										
n-PENTANE	107										
HEXANE	482										
n-HEPTANE	124										
SUBTOTAL	20,503										
PENTENES	973										
DICYCLOPENTADIENE	64										
GRAND TOTAL	96,010										

+includes:

BUTADIENE	2,340
2-BUTENES	640
1-BUTENE	414
ISOBUTYLENE	303

*includes

p-XYLENE	4,779
XYLENES	4,464
o-XYLENE	675

** Included with aromatics because of tradeoff with benzene.

PART III

The Biomass Alternative

A National Insurance Policy To Protect the U.S. Strategic Supply of Chemical Feedstocks

The market study was aimed at helping to define a strategically relevant national plan for developing new processes to convert renewable resources to organic chemicals by indicating significant avenues for process research. In the preceding section an assessment was made of present petrochemical products and their interrelation among themselves and their generic feedstocks. In this section this product position is extrapolated to a biomass feedstock economy based on technically demonstrated, albeit presently economically unfavorable, processes. To do this the data base was reorganized relative to alternative routes to feedstocks or derivatives based on renewable resources.

1. Historical Perspective

Prior to the post-World War II boom in the chemical industry, many of the high volume chemical feedstocks were made from sugar substrates by fermentation. These included basic chemicals such as ethanol, from which ethylene and butadiene were made, butanol, acetone, acetic acid, etc.

However, following the war, low cost petroleum and natural gas became available in the early 1950's. As a result the introduction of cheap petroleum feedstocks was more or less the death knell of the fermentation industry as people knew it at that time. For the next 30 years, the chemical world became basically synonymous with producing petrochemicals from crude oil and natural gas-based feedstocks.

When the big energy crunch of 1973 occurred, many in the chemical process industry started to consider alternatives. Some reassessed the possibility of producing chemicals from *coal*, air and water (again). Others opted to investigate a future of producing chemicals from *sunlight*, air and water using photosynthesis to produce the basic carbohydrates needed as a source of energy and fixed carbon for these oxychemicals. For a decade then, industry and academia, supported by Federal energy programs, explored ways to prepare cheap "biosugar" feedstocks from lignocellulose in the form of tree chips or agricultural residues and to convert such renewable raw materials into chemicals of fuels.

Unfortunately for these programs, the softness in crude oil prices that occurred in the early 1980's brought an end in most cases to research programs aimed at using renewable resources as a basis for chemicals.

2. National Insurance Policy Concept

Although the chemical industry has abandoned interest in renewable programs—at least for the moment—it is not to say that the same strategic shortfall in *cheap* petroleum feedstocks will not return. Indeed, James E. McNabb of Conoco, a leading petroleum refiner, pointed out that while OPEC was operating at 60% of capacity in the 1980's, it will reach 80% of capacity early in the 1990's. Then, market power will shift from consumer to supplier with a resulting trend toward raising prices again. As a consequence he forecasted that although oil prices will remain in the low $20's in the early 1990's, they will rise to the mid-$30's by 1995 and to $50 per barrel by the year 2000 [1,2] (fig. 2). In contrast, the cost of corn, a major biomass supply, is currently at $1.50-$2.00 per bushel—about where it was in 1970 (fig. 9) [3-6].

Already, considerable pressure is being placed on the price of ethylene as a result of a strong demand for the plastics: polyethylene, polyvinyl chloride, and polystyrene [7]. This pressure led to an increase in ethylene prices to 15.5 cents per pound in September, 1987. It is expected that the industry will operate at above 95% of the average nameplate capacity of 35.2 billion pounds in 1987.

Price pressure on the other olefins has also been severe. The price of propylene reached 18 cents per pound in September, 1987 compared with 10 cents at the beginning of the year as a result of

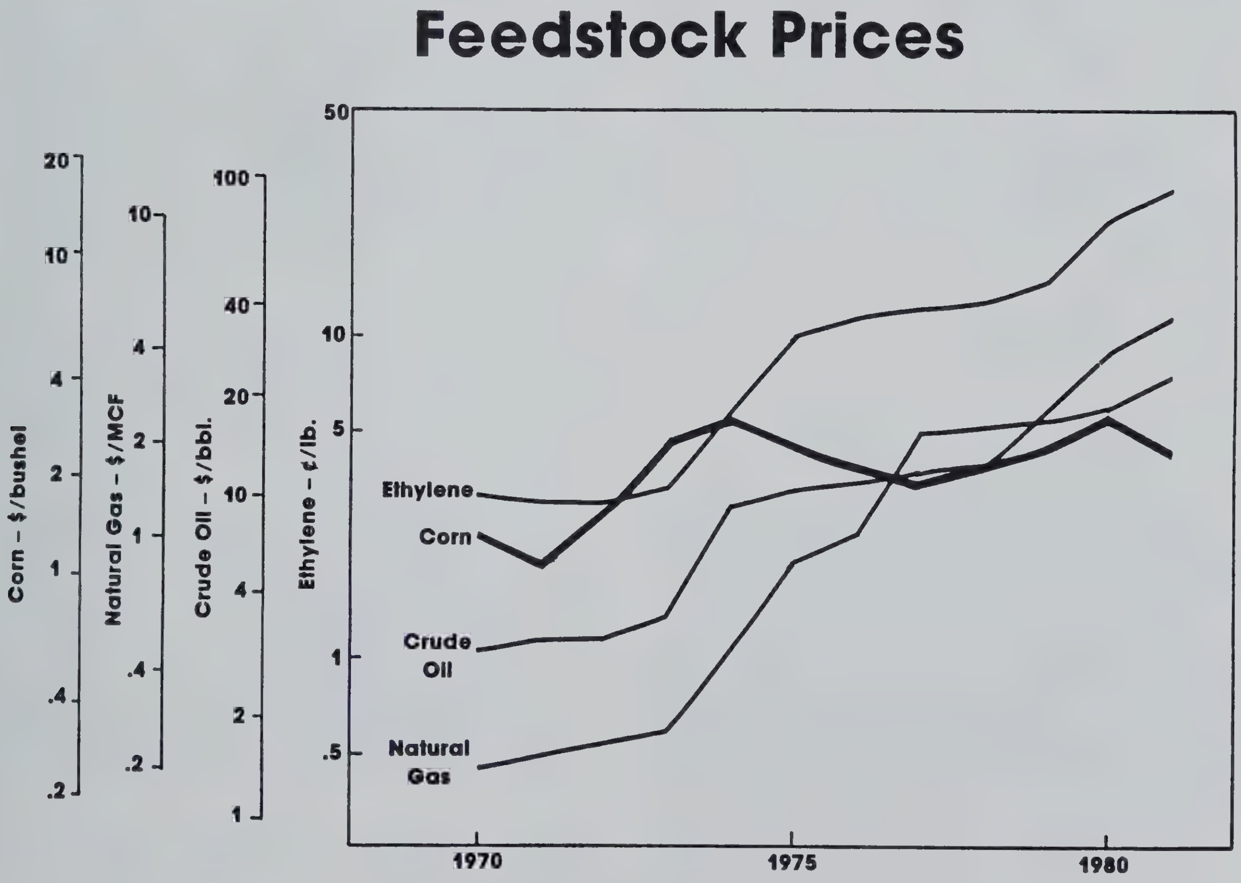


Figure 9

increased demand for polypropylene. Similarly, butadiene prices increased to 30 cents per pound from a low of 9 cents in October, 1986. Such trends may be bellwethers of future price increases since tight supplies are expected to continue over the near future.

In addition, while the American chemical industry scrambles to reposition its businesses into more lucrative specialty chemical markets, the Saudi ministers have repeatedly announced their intentions to invest heavily in commodity chemicals production. Already, Union Carbide, a leading supplier of synthetic ethanol in this country, is having ethanol produced in Saudi Arabia on a toll basis [8]. Nevertheless, E.C. Holmer, the recent president of Exxon Chemicals, sees no real threat in the commodity chemical capacity being built close to the Middle East wellheads [9]. He points out that there is nothing cheap about petrochemical operations in remote Middle Eastern countries. Construction costs are tremendous and operating costs are very high, as are transportation charges for moving products to established markets. On the other hand, ethylene produced by the Saudi Basic Industries is based on its no-value, excess associated gas which is otherwise flared. Since over half the cost plus return for ethylene is based on raw material costs, this is a formidable advantage; particularly if the price of crude oil rises from the current $20 per barrel to $35 again or more.

In the meantime, it would be a nationally tragic waste of scientific momentum if some programs on biomass-based chemicals were not kept alive as a strategic insurance policy when and if the Middle East economic and political climate triggers another and probably far worse crisis in petroleum feedstocks.

3. Bio-Product Market Potential

The biomass-oriented database was compiled by applying the biomass process scenario, described in a later section, to the need for chemicals. The data are sorted for all products and for each of the major feedstocks and their derivatives. The results are summarized in Table 11.

Table 11

THE BIOMASS ALTERNATIVE
INTER-RELATION AMONG POTENTIAL FEEDSTOCKS

(MILLION POUNDS PER YEAR - 1985 BASIS)

	PRIMARY FEEDSTOCK	----DERIVATIVES----	
		SINGLE FEEDSTOCK	FEEDSTOCK COMBO´S
ETHANOL	5,352	103,351	55,448
PROPANOL	1,235	31,588	24,284
BUTANOL	716	3,693	3,068
ACETONE	1,788	1,177	5,000
ACETIC ACID	2,917	0	5,630
FUMARIC ACID, ETC.	923	1,051	165
POLYHYDRIC ALCOHOLS	760	1,923	4,509
SUBTOTAL	13,690	142,784	98,104
SYNTHESIS GAS	0	23,750	20,554
AROMATICS	29,873	9,928	67,331
SUBTOTAL	29,873	33,678	87,885
NATURAL PRODUCTS	0	2,586	4,454
PETROLEUM PRODUCTS	21,549	0	0
GRAND TOTAL	65,112	179,048	71,816 *

* By difference; column does not add because of duplications within derivative combinations.

Biomass sources could account for almost all of the current petrochemicals except for 21 billion pounds of petroleum products that are predominantly C2-C7 alkanes. These petrochemicals would be replaced by biosugar as feedstocks for ethylene, etc. Hence, bioproducts could constitute 294 billion pounds of products or 93% of the total; valued at roughly $106 billion dollars. As shown in figure 10 this amount exceeds the 1985 personal purchase of new automobiles in the United States and is 68% as large as clothing purchases. It represents 6.5% of the gross national product for goods and 2.5% of the total GNP for 1985.

The markets for "bioproducts" that might be produced from renewable materials are listed in Table 12 [10]. Overall values are shown for world sales, except for selected commodity organic solvents and acids, which are shown only for the United States. These commodity oxychemicals comprise a U.S. market volume of about $14 billion. For the rest of the products listed, sales are an order of magnitude lower. At the bottom of the list are some of the newer products of biotechnology, like genes and whole cells, for which markets are very promising, but yet to develop. The materials in the middle of the chart comprise explosive markets that are now opening for products such as polypeptides and new hormones produced by recombinant methods.

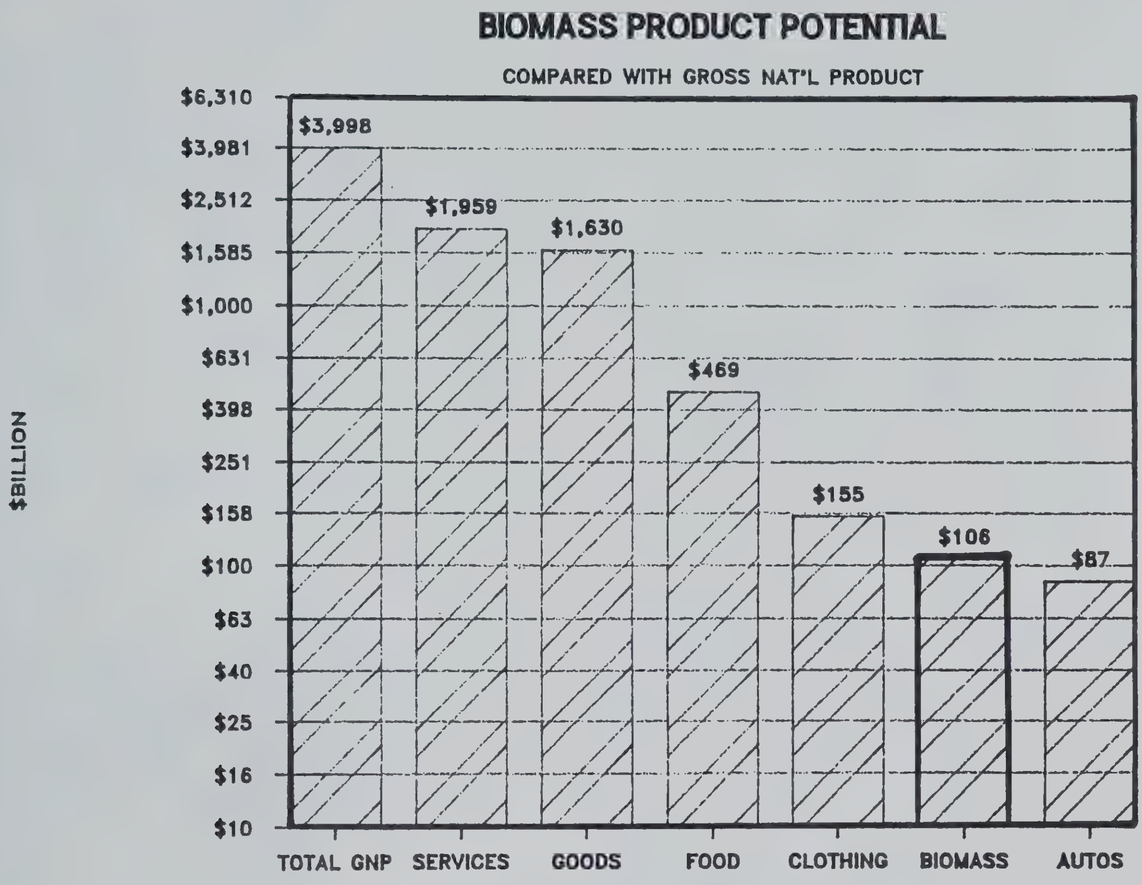


Figure 10

Table 12 Bio-Product Markets

Current World Sales ($ Million)	Product
$14,180 (USA)	Organic Solvents & Acids*
1,700	Amino Acids
1,625	Antibiotics
667	Vitamins
440	Industrial Enzymes
380	Steroids & Alkaloids
260	Polypeptides & Hormones
160	Nucleotides, Nucleosides
155	Medicinal Enzymes
—	Biopolymers
100	Polysaccharide Gums
—	Genes > 1MM MW
—	Cells

*Current and potential applications

3.1 Primary Oxychemical Feedstocks

3.1.1 Ethanol Since it was assumed that ethylene would be produced by dehydrating ethanol, it is understandable that ethanol would become the ranking biomass-based feedstock. Moreover, butadiene would also be produced from ethanol as it was during World War II by Publicker and Union Carbide in government plants to provide synthetic rubber for the war effort. Accordingly, ethanol would capture an even greater share of the total feedstocks than ethylene does for petrochemicals. It should be pointed out that the data for ethanol as a primary feedstock in Table 11 refer to the amount of ethanol now produced rather than that which would be needed to produce the derivatives that would be attributed to it.

3.1.2 Ethanol Derivatives As shown in figure 11, potential ethanol derivatives could account for a third of all organic chemicals, while propanol derivatives could account for another 10%.

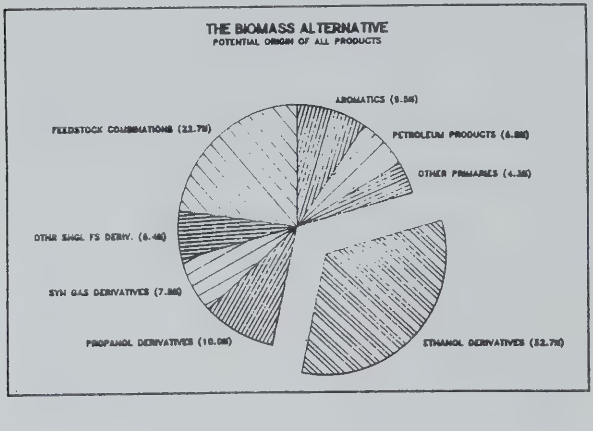


Figure 11

A further breakdown of derivative combinations is shown in Table 13 and figure 12. Of all derivatives, those based on ethanol alone comprise the largest share. Derivatives of ethanol with aromatics are in a substantial second place (fig. 13). A dual research program on ethanol fermentation and lignocellulose hydrogenation would be required to achieve this position. Derivatives of propanol and synthesis gas, either alone or in combination with other primary feedstocks also appear to be important.

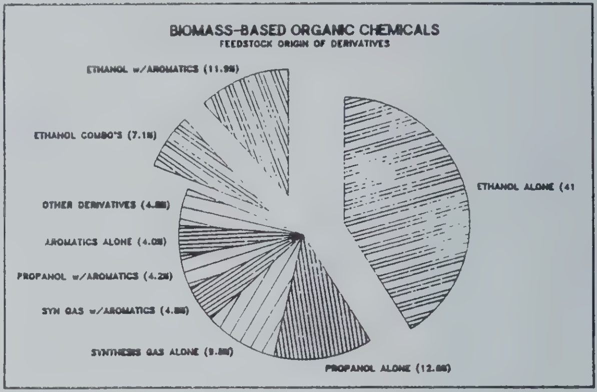


Figure 12

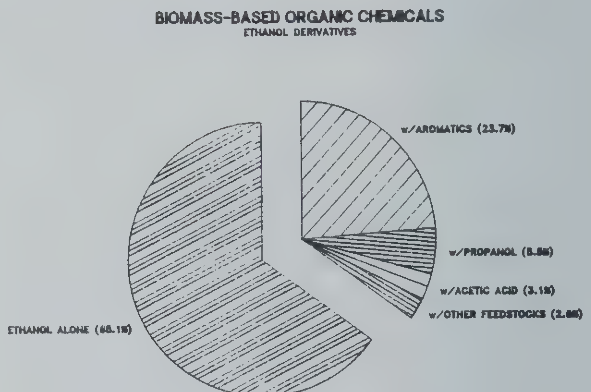


Figure 13

Table 13

THE BIOMASS ALTERNATIVE
INTER-RELATION AMONG POTENTIAL F EEDSTOCKS
(MILLION POUNDS PER YEAR - 1985 BASIS)

	PRIMARY	DERIVATIVES WITH OTHER FEEDSTOCKS										
	FEEDSTOCK	ETHANOL	PROPANOL	BUTANOL	ACETONE	ACETATE	FUMERATE	POLYOLS	SYN GAS	AROMATICS	NAT PROD	TOTAL
THANOL	5,352	103,351	8,717	79	535	4,850	0	272	1,819	37,695	1,483	158,800
ROPANOL	1,235	8,717	31,588	504	421	406	0	396	2,454	10,625	761	55,872
UTANOL	716	79	504	3,693	0	179	3	357	1,898	48	0	6,761
CETONE	1,788	535	421	0	1,177	0	0	0	2,011	2,030	3	6,177
CETIC ACID	2,917	4,850	406	179	0	0	0	103	0	28	63	5,630
UMARIC ACID, ETC.	923	0	0	3	0	0	1,051	0	0	158	4	1,216
OLYHYDRIC ALCOHOLS	760	272	396	357	0	103	0	1,923	188	2,933	261	6,432
SUBTOTAL	13,690	117,804	42,032	4,815	2,133	5,538	1,054	3,050	8,371	53,517	2,574	
YNTHESIS GAS	0	1,819	2,454	1,898	2,011	0	0	188	23,750	12,059	124	44,303
ROMATICS	29,873	37,695	10,625	48	2,030	28	158	2,933	12,059	9,928	1,755	77,260
SUBTOTAL	29,873	39,513	13,080	1,946	4,041	28	158	3,121	35,809	21,987	1,879	
ATURAL PRODUCTS	0	1,483	761	0	3	63	4	261	124	1,755	2,586	7,040
ETROLEUM PRODUCTS	21,549	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL	65,112	158,800	55,872	6,761	6,177	5,630	1,216	6,432	44,303	77,260	7,040	

Depending on relative economics, ethanol from biomass might someday, but probably not before the year 2020, compete with heavy hydrocarbon feedstocks as a raw material for ethylene and butadiene. World War II processes for accomplishing this have already been introduced into Brazil's ethanol-based energy economy. However for the free market economy of the United States, the dehydration processes suffer from inherently poor raw material stoichiometry, expressed in the maxim: "Don't remove H_2O from CH_2O."

3.1.3 Other Oxychemicals Hence, it seems more reasonable to expect that as fossil fuels become more expensive, both cellulose and starch could become increasingly more important as cheap raw materials for oxychemicals that retain the oxygenated nature of the glucose monomer units of biomass. Against the background of the present synthetic organic chemicals industry, the 16 top oxychemicals listed in Table 14 have been, are being, or could be produced from renewable materials rather than fossil materials. All except adipic acid, 1,4-butanediol and methylethylketone are primary feedstocks in the sense that they can be produced directly from biosugar.

These oxychemicals from renewable resources could account for 50 billion pounds, 24% of the production of the top 100 chemicals. Their derivatives could account for another 26%, for a total production of half that of the top 100 chemicals.

OXYCHEMICALS MARKET POTENTIAL
(million pounds)

	Without Olefins	With Olefins *
Primary Compounds	17,260	50,060
Derivatives	12,530	55,620
Total	29,790	105,680

* Ethylene and butadiene ex ethanol

Certainly, the United States and the world already have an ample production capacity to supply current needs for such feedstocks [11](see Table 15). However over the past 5 years alone, there was a need for a considerable increase in U.S. or world production capacity:

	U.S.A.	World
Ethylene	+14%	+31%
Butadiene	+30%	+26%
Ethylene Glycol	+26%	+33%

Table 14

OXYCHEMICAL MARKETS FOR INNOVATIONS IN BIOTECHNOLOGY

	Current US Value ($ Million)
Ethanol	
—Ethylene	$ 6,790
—Butadiene	1,320
—Octane Enhancer	560
—Industrial	380
	9,050
Ethylene Glycol	1,260
Adipic Acid	1,030
Acetic Acid	620
Isopropanol	500
Acetone	460
Acrylic Acid	360
Glycerol	250
1,4-Butanediol	240
Propylene Glycol	220
Methylethylketone	210
n-Butanol	200
Citric Acid	190
Sorbitol	90
Propionic Acid	35
Fumaric Acid	25
Total Oxychemicals	$14,180

Source: US ITC

Table 15

Production Capacity

(Million annual pounds)

	United States	Western Europe	Japan	World
Ethylene	36,300	36,000	12,700	104,500
Ethylene Glycol	5,380	2,970	1,370	12,220
Butadiene	4,020	4,600	1,620	12,530
Acetic Acid	3,540	2,540	1,450	8,520
Acetone	3,290	2,390	620	6,890
Isopropanol	2,800	–	–	–
Ethanol	2,510	1,240	260	17,860*
Adipic Acid	1,910	2,350	150	4,930
Propylene Glycol	870	820	15	1,920
Methyl Ethyl Ketone	870	570	140	1,800
n-Butanol	800	–	–	–
1,4-Butanediol (& THF)	380	220	20	620
Glycerol	340	470	120	1,010

*Includes 5930 MM lbs. – USSR; 5580 MM lbs. – Brazil

For future expansions, oxychemical plants based on renewable materials would need to compete on a grass-roots basis with new fossil-based plants. To penetrate beyond this, new renewable-based plants would have to slug it out with incumbent fossil plants. Overall though, in the long term inexorable pressure of rising OPEC oil prices will generate a need for alternative sources of fuels and chemicals.

4. Marketing Position

Marketing position relates to a company's ability to deliver a product to the market place. A lot depends on whether the products are produced for captive use, or are intended for the merchant market. Another consideration is whether the product is a specialty chemical, which can command a high price but usually requires a large amount of product support, or a commodity chemical, which requires a competitive price advantage resulting from process technology at the cutting edge of science.

In considering specialties, a company like Staley might decide, as it did, to produce glucosides for the merchant market. Conversely, companies like Pfizer might consider market opportunities leading from existing products they currently produce from corn syrup.

On the other hand, from the point of view of commodity oxychemicals, companies in this area would probably approach the opportunity from the point of view of captive use. This use involves the change from a fossil-based process to a cheaper renewable-based process, rather from the point of view of entering a merchant market new to the company. A possible exception might be ethanol, which has a government supported place of its own at the moment as an octane enhancer of gasoline.

Price is obviously a strong determinant. As shown in figure 4, price is inversely related to market volume. Specialty chemicals and pharmaceuticals command high prices but low volumes.

Marketing position is a prerequisite to success in a new venture. Each company has to judge for itself where its position lies or could be developed in that scheme of things. A small technically skilled startup business would probably be more successful in directing its research toward specialties rather than commodities. However, it could enter a larger volume market through an alliance with a larger company that could contribute a manufacturing and marketing capability to the joint venture. An example of this is the joint venture: Ecological Chemical Products Company, recently announced between ConAgra and the Dupont Company to produce biodegradable polylactide polymers.

5. Product Position

Product position refers to a company's ability to maintain a monopolistic control of the market through strong product patents or specialized proprietary knowhow. A company involved in specialty markets usually has some product position, since the very name suggests that production is limited and the market cannot support too many competitors.

However, in term of commodity feedstocks, there can be no product position. Such materials are all well-known chemicals. Proprietary product patents have long since expired, and only a weak process patent position is possible. Companies entering these markets will need to develop both a raw material position and a manufacturing position to be successful.

6. Raw Material Position

One of the most important aspects of a commodity chemical business is that of raw material position. There are two basic renewable feedstocks in nature of interest here: starch and lignocellulose. In practical economics, starch in the United States refers almost exclusively to corn starch; while lignocellulose refers to wood chips or, to a lesser extent, corn stover or cereal straws.

6.1 The Nature of Biomass

Biomass comprises collectible, plant-derived materials that are abundant, inexpensive and potentially convertible to feedstock chemicals by fermentation or chemical processes. It is found as starch, a polymer of glucose, in corn, wheat, potatoes, cassava, the sago palm, and other agricultural products. It is found as monomeric sugars or soluble oligomers in corn syrup, molasses, raw sugar juice, sulfite waste liquors, etc. Biomass also occurs as lignocellulose in the form of wood chips, crop residues, forest and mill residues, urban refuse, or animal manures. Cellulose, like starch, is also a high polymer of glucose.

Lignocellulose is the structural material of plants. More complex than starch, it is a composite of three polymers (see Table 16). In wheat straw and hardwoods these comprise: 42% cellulose, a linear polymer of glucose that occurs as microfibrils; 35% hemicellulose, an amorphous, branched copolymer comprised mainly of xylose; and 22% lignin, a cross-linked polymer of substituted phenylpropane units [12,13].

Table 16

Composition of cellulosic materials (% dry, extractives-free)

	Soft Woods	Hard Woods	Wheat Straw	Bagasse	Corn Stover
α-cellulose	43.8	42.4	42.4	38.7	42.8
Hemi-cellulose	26.5	35.6	33.5	39.0	42.0
Lignin	29.5	21.7	22.5	20.6	14.0
Ash	0.2	0.3	1.6	1.7	1.2
Polysaccharides					
-C_6	56.6	51.1	45.8	46.2	49.0
-C_5	6.9	18.2	24.6	27.0	25.6
-Total	63.5	69.3	70.4	73.2	74.6

Chemically, almost all biomass regardless of source, contains about 45% oxygen on a moisture and ash-free basis [12,13] and most also contains 50% moisture as collected (Table 17). Thus, biomass makes a poor fuel. With 50% moisture, materials such as sugarcane bagasse have a net heating value as received of only about 6,800 Btu per pound (dry basis)—or about half that of bituminous coal [14]. Government programs to the contrary, cellulosic biomass is a poor choice as an energy source, unless it is a waste material that must be disposed of at least cost. However, starch, sugar or lignocellulose have potential as feedstocks for oxychemicals that retain the oxygenated nature of the basic CH_2O structure.

Conversely, it would be much more difficult economically to attempt to squeeze H_2O out of CH_2O. For example, in dehydrating ethanol to ethylene, the molecular weight is reduced from 46 to 28. This means that water worth about $1.80 a gallon as ethanol is discarded. The situation obviously makes for poor economics. One might hedge a bet on this by noting that back in the early 1980's one might have, in fact, considered doing this because of the fantastic rate of rise in the cost of ethylene. Now, however, with the softness in that market, the economics of producing olefins from ethanol look dim for the foreseeable future [15].

Three general conclusions can be drawn from these basic considerations: (1) If you want to provide energy, aromatic chemicals, or methane/syn gas, buy your self a coal pile; (2) However, if you are looking for oxychemicals that maintain the oxygenated nature of the glucose molecule, then you might seriously consider biomass; (3) Finally, if you need olefins, biomass might be a possible source, but one needs to take a very hard and critical, albeit long term, look at such apparent opportunities.

6.2 Biomass Supply

As a product of solar energy, the biomass supply depends on the land dedicated to useful photosynthesis. Of the total 2.3 billion acres of the United States, 380 million acres, or 17%, are devoted to crops; 720 million acres, or 32%, to forest and woodland; and 680 million acres, or 30%, to pasture or grazing land [16].

Of all American crops, corn is the primary source of starch because of its ample supply, low cost relative to other sources of starch or sugar, and established commercial systems for storing and transporting the grain cheaply over long distances. Corn yields over recent bumper corn crop years have amounted to 7-8 billion bushels, equivalent to 225-250 billion pounds of starch or 250-275 billion pounds of sugar [5,17].

Table 17

Biomass elemental analysis — wt%

	Pine Wood	Bagasse	Corn Cobs	Urban Refuse	Feedlot Manure	Giant Kelp
Ash (d.b.)	0.5	2	1	14	24	39
Moisture	50	50	7	18	70	90
Ash-free dry solids						
Carbon	52	47	44	48	46	45
Oxygen	41	46	48	45	43	46
Hydrogen	6	6	8	6	7	6
Sulfur	0	<.1	<.1	0.2	0.5	0.6
Nitrogen	0.1	0.5	0.6	0.6	3.3	2.0

In contrast the annual *collectible* supply of lignocellulose amounts to almost 800 million dry tons, equivalent to 1.1 trillion pounds of polysaccharides [18-20]. This lignocellulose supply is about equally divided between collectible residues of the major agricultural crops and annual available growth of American forests net of commercial removals and mortality [21].

Lignocellulosic crop residues are abundant, but commercial collection systems are limited and need to be developed to exploit this potential resource. Only eight million annual dry tons of crop residues, such as sugarcane bagasse, cotton gin trash, and rice hulls, are presently collected at certain processing sites (see Table 18). About 105 million annual dry tons of corn stalks and 180 million annual dry tons of cereal straw are available and could be collected if the demand warranted it. The additional potential supply of 525 million dry tons of other agricultural residues is too diffuse to be collected economically or must be retained on the land to maintain the soil.

Table 18

U.S. cellulosics potential — Cropland resource (Million annual dry tons)

	Collected Supply	Collectible Reserve	Potential Resource
Corn stover	–	105	212
Cereal straw	–	180	180
Soybean residues	–	25	50
Bagasse, gin trash & rice hulls	8	–	8
Other crops	–	–	360
Total cropland	8	310	810

The annual growth of the American forests could provide an economically collectible supply of 270 million annual dry tons of lignocellulosic biomass (see Table 19). This amount is net of mortality and commercial removals from a commercial inventory of 25 billion tons of standing tree stems. Eastern hardwoods, which are of lesser importance to the pulp and paper industry than the stronger-fibered conifers, are primary target sources [19,20].

Urban solid waste is the ultimate end for paper and board products. This source might supply another 30 million tons from the 32 largest urban centers. The supply from each of these would exceed the 400,000 annual dry tons needed for a cellulose-based chemicals plant [22-23]. However the heterogeneity of these materials raises safety and process problems in downstream operations.

Table 19

U.S. cellulosics potential – Forest resource (Million annual dry tons)

Forest	Collected Supply	Collectible Reserve	Potential Resource
Net annual growth*	–	270	450
Logging residues	–	105	145
Process residues & wastes			
— Pulp mills	3	38	46
— Saw mills (excl. chips)	13	13	26
— Paper & board mills	–	12	13
Fuel wood	3	–	3
Urban solid wastes	41	12	77
Total Forest	60	450	760

*Net of mortality and removals ex commercial inventory of 25 billion tons

The "grassland" cellulose resource, mainly animal manure (see Table 20), is too diffuse, except for a few large feed lots, to be a source of lignocellulose for chemicals [24,25].

Table 20

U.S. cellulosics potential — Grassland resource (Million annual dry tons)

	Collected Supply	Collectible Reserve	Potential Resource
Cattle	5	4	237
Hogs	–	–	11
Broilers	–	–	6
Chickens	–	2	4
Sheep	–	–	2
Total grassland	5	6	260

Hence, from a potential supply of 1.8 billion annual dry tons of lignocellulose from U.S. cropland, forest, and grassland, the 550 million dry tons of biomass available as wood chips, cereal straw and corn stalks, and the starch from 190 million tons of corn grain appear to be the most viable sources upon which to build a chemicals-from-biomass industry. As yet, cereal straw and corn stover—the major agricultural residues—have no infrastructure for collection and business manipulation. So, for the moment, corn and wood chips must be considered as the only renewable materials currently available in large supply.

In summary, the total U.S. biomass supply is roughly four times greater than the volume of petrochemicals now being produced. This is not a very large surplus considering that the entire United States corn crop and forest growth is involved. One can conclude that other resources, such as coal, will be important adjuncts to biomass use.

6.3 Geographical Distribution

In contrast to coal which occurs in a three-dimensional sense as thick seams in many stripmined areas, biomass occurs as a two-dimensional, diffuse supply, spread over the land from which it is derived. The geographical distribution is shown in figure 14.

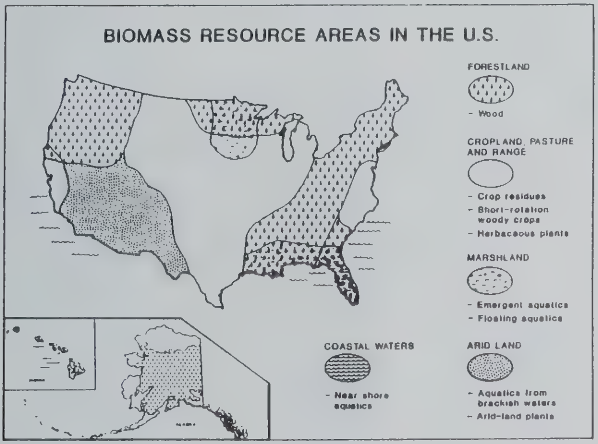


Figure 14

Most of the corn and wheat, and the residues from these operations, is grown in the heartland of the United States. A study was made by the author some years ago to identify potential locations for plants that could supply 400,000 dry tones of agricultural residues within various radii of a plant site. Figure 14 shows the situation for a 40-mile radius. It was assumed that only 50% of the available biomass on an area-average basis would be removed from the land. The remainder would be left to provide humus and prevent soil erosion. Any one of these sites could theoretically support the production of at least a million pounds per day of biosugar by hydrolysis of the cellulosic biomass. The index shown on the chart gives some idea of supply volume. The sites identified by very small dots could supply 400 million dry tons annually. Much larger supplies would be available in other areas.

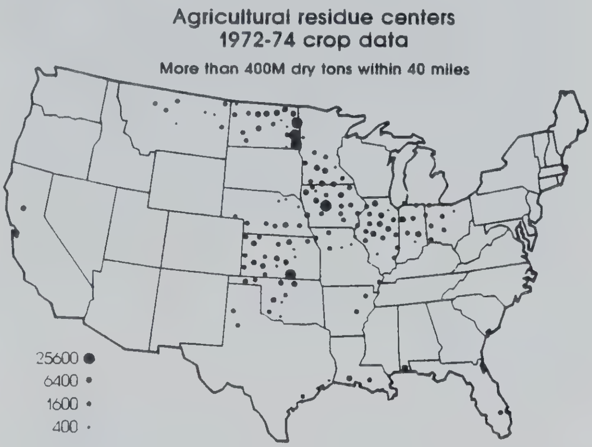

Agricultural residue centers
1972-74 crop data
More than 400M dry tons within 40 miles
25600 ●
6400 •
1600 •
400 ·

Figure 15

The timber resource is also vast (see Table 21)[18]. Hardwoods are basically located in the Northeast, Northcentral and South, but very little in the West. Hardwoods are generally less desirable than conifers to the pulp and paper industry because they have short, weak fibers. Hardwoods are preferred, however, for chemical use since they contain less lignin and tacky, dirt-collecting extractables. Presumably they could be used without seriously competing with the pulp and paper industry for raw materials.

Table 21

U.S. Timber Inventory
(Million dry tons)*

	Hardwood	Softwood	Total
Northeast & Central	1920	530	2450
South	1340	1070	2410
Pacific Northwest	250	3110	3360
Rockies	70	1210	1280
Total	3580	5920	9500

*"Commercial" standards

6.4 Supply Versus Need

How do these raw material supplies compare with the total potential need for chemicals? The biomass needs for producing various oxychemicals are shown in Table 22. Except for the olefins: ethylene and butadiene, the entire U.S. supply of major oxychemical feedstocks could be produced from only 11% of the corn supply. That is about the amount of corn that corn refiners presently use annually. Likewise it would only take about 3% of the available excess cellulose to do the same job. Clearly, there is an ample raw material supply available for at least these major products, provided that a business system can be developed to get the biomass to the right place at the right price.

Table 22

Oxychemicals from renewable resources

	Production MM lbs.	% Corn crop.*	% Cellulosic biomass**
Ethanol			
– Ethylene	29,200	36.5	9.5
– Butadiene	3,600	5.3	1.4
– Industrial	1,310	.9	.2
Ethylene glycol	4,600	1.6	.4
Acetic acid	3,300	1.3	.3
Acetone	2,500	2.7	.6
Isopropanol	1,970	2.1	.5
Adipic acid	1,800	1.4	.3
n-Butanol	560	.6	.2
Propylene glycol	550	.2	.05
Glycerol	370	.1	.03
Butanediol & THF	300	.3	.1
Sorbitol	130	.04	.01
Total excluding olefins		11%	3%

*7.4 MMM Bu.

**770 MM dry tons – Collectible supply

6.5 Opportunity for Cooperative Enterprises

It seems quite likely that traditional chemical companies, based over the past thirty years on petro feedstocks, would make only a reluctant transition to the purchase of corn and the hydrolysis of starch to produce their raw materials. That is, however, the business of the wet milling industry. Accordingly, dialogue between wet millers and chemical companies may open the door to a further cooperation between the two industries to get the whole job done. A similar cooperative effort might be developed with the pulp and paper industry for the hydrolysis of cellulosic materials.

7. Conversion Process Scenarios

In the conversion of biomass to chemicals two basic process considerations must be addressed: (1) whether starch or lignocellulose feedstocks are to be used directly or hydrolyzed to a "biosugar" syrup amenable to further processing; and (2) what process is to be used for the conversion of the substrate to the chemical product. A "biorefinery" system for processing renewable biomass is shown in figure 16. Many options are available.

Feedstocks from renewable resources

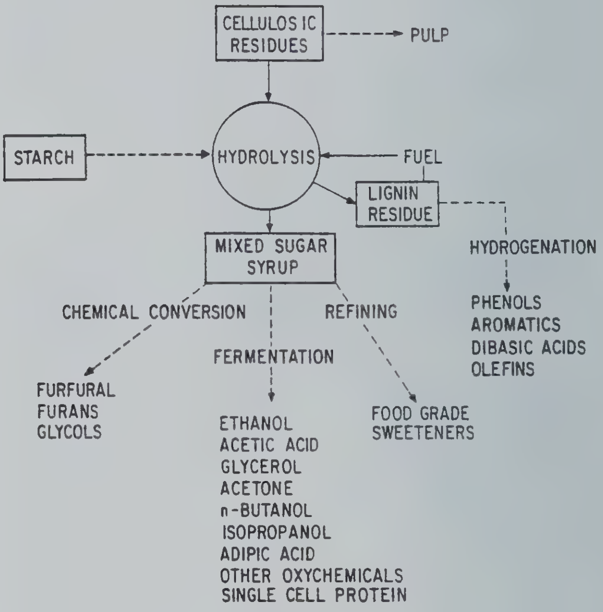


Figure 16

One could start with corn as the wet process corn industry does, hydrolyze the starch to a crude sugar syrup, and then refine and further process the syrup to provide food-grade sweeteners, such as high fructose corn syrup. Corn starch, certainly at present, and cellulose, potentially, can be hydrolyzed by acid [22-36] or enzyme catalysts [37-39] to produce sugar mixtures. The crude sugars can be further converted by *fermentation* or *hydrogenolysis* to chemicals.

Alternatively, one could start with cheaper lignocellulosic materials, hydrolyze these, and process the biosugar in a similar manner. In this case a lignin/cellulose residue would be produced that could be used as a fuel in the plant, as is currently done with bagasse in raw sugar factories, or could be further processed.

In the hydrolysis of cellulosic materials, the biosugar product is a mixture of sugars, principally glucose and xylose if hardwoods are used. These might be separated and processed separately. For example, xylose might be used to produce the sweetener xylitol by fermentation or could be chemically converted to ethylene glycol [40-42] or to furfural and furans as the Quaker Oats Company used to do [43,44].

Lignocellulosic materials can also be *gasified* directly to produce synthesis gas (a mixture of carbon monoxide and hydrogen) in a manner similar to coal gasification. They can also be *hydrogenated*, as coal can be, to produce a mixture of oxygenated aromatic compounds [45]. In fact, lignin, the geological precursor to coal, might be considered the ultimate source of aromatic chemicals.

As a plausible scenario it was assumed that all four of the above conversion processes would be employed in the "biomass alternative."

7.1 Fermentation

Fermentation could be used to produce the following products from biosugar:

(1) Ethanol via the yeast *Saccharomyces cerevisiae* or bacterium *Zymomonas mobilis*. The commercial yeast system is relatively satisfactory with respect to product concentration in the beer but needs to be improved with respect to increasing fermentation rates [46,47]. *Zymomonas* shows promise for outstanding performance if operating consistency can be demonstrated [48].

(2) Isopropanol, n-butanol, and acetone via the bacterium *Clostridium acetobutylicum* or its mutated counterparts. The product concentration attainable in this system is severely limited by product feedback inhibition, which must be corrected [49]. The innovations made by Battelle Memorial Institute in its in situ extractive fermentation process for butanol appear to have the profound effect of increasing effective concentration of product to 140 g/l while maintaining actual concentration near the organism below 10 g/l, the threshold of inhibition [50]. As a result, the selling price to yield a 30% pretax return on investment might be reduced from over $1.25 per pound for butanol if produced now by the old Weizmann process to about 59 cents per pound. Further reductions appear attainable.

(3) Acetic acid via *Acetobacter suboxydans* from ethanol in a modernized version of the old vinegar process or directly from sugar via *Clostridium thermoaceticum*. The vinegar organism provides acceptable concentrations of acetic acid (10%) in the beer but requires a two-step fermentation by way of ethanol. As a result, theoretical yield is limited to two mols of acid per mol of glucose [51]. The product concentration of the newer *Clostridium* system is woefully limited by product inhibition, although theoretical yield is three mols of acetate per mol of glucose [52,53].

(4) Fumaric acid or malic acid via the fungus *Rhizopus arrhizus*. Both yield and product concentration have been exceptional in laboratory studies, but further demonstration at pilot scale is needed [54].

7.2 Hydrogenolysis

Hydrogenolysis of glucose is the preferred route to commercial sorbitol. It was extensively studied years ago as a route to the polyhydric alcohols: glycerol, ethylene glycol, and propylene glycol [40,41]. However, cheaper petroleum substrates redirected research to the synthetic routes. More recent improvements to the catalyst system [42] could lead to a practical process for producing ethylene glycol.

Alternatively, glycerol could be produced directly by fermentation [55]. The glycols can also be produced via fermentation to the respective alcohols followed by dehydration to the olefin and vapor phase oxidation to the oxide. Hydration of the oxide is the current commercial method. Hence in this study, products from hydrogenolysis can be compiled separately or lumped under the alternative fermentation route.

7.3 Gasification

Many studies of the gasification of biomass have been made over the past decade and earlier. In gasification part of the raw material is burned to provide energy for the endothermic gasification reactions. Unfortunately biomass usually contains 50% moisture as received and 45% oxygen on a dry basis. Both place a severe thermodynamic handicap on the use of biomass compared with coal [12-14]. On the positive side biomass is usually sulfur-free, so that gas cleanup is much easier and cheaper to accomplish. Whether this attribute can overcome the basic composition shortcomings remains to be seen. In any event, synthesis gas from either biomass or coal could be teamed with the other conversion routes to spare the use of natural gas for this purpose.

7.4 Hydrogenation

The production of aromatic compounds from coal or biomass has very early beginnings in the German Bergius process. This approach was further developed during the energy crises of the early 1950's and 1970's [56]. The process is embodied in the highly successful H-Coal process program. The so-called Lignol process is the biomass spin-off. The latter process has shown a 38 wt% yield of Kraft lignin to phenols consisting of: 2.5% phenol, 9.5% cresols, 12.5% ethyl phenol, 10.5% propyl phenol, and 2.6% xylenol. It was expected that a commercial plant could produce 98 t/d of phenol, 70 t/d benzene, and 53 t/d fuel oil from 485 t/d Kraft lignin [45,57].

Coal provides a product slate of the preferred non-oxygenated aromatic compounds and would be a better raw material for this purpose if cost is comparable to biomass.

8. Competitive Cost Advantage

Developing a competitive cost advantage is the bottom line for a commodity chemicals business. To evaluate competitive advantages for any scheme developed from the "biorefinery" overview, one needs to examine the *cost of raw materials* relative to *conversion costs* for the process alternatives.

8.1 Raw Material Costs

Certainly raw materials costs are a big share of total cost. By way of example, the cost of producing ethanol from corn is shown in Table 23. These figures are for a 25 million gallon batch-process plant operating in 1980. At that time, plant investment was roughly a dollar a gallon. It is higher now, and more recent estimates are discussed later in this report. However, these data make the point that corn net of grains credit costs $0.60 per gallon out of a $0.97 per gallon mill cost and a $1.42 per gallon cost-plus-30% pretax return. Consequently, the cost of raw materials is of paramount importance. This cost is comprised of two factors: the yield of product on raw material and the price of the raw material. Yield will be discussed later in connection with specific product systems.

Table 23

Economics – Ethanol from corn (1980 dollars)

Basis
  25 MM GPY 190° alcohol
  Batch process
  2.86 gallons/bushel

Investment – $29 MM

Cost – $/gallon	
Corn @ $3.00/bu.	$1.05
Grains credit @ $140/ton	(.46)
Steam – alcohol recovery	.10
– grains recovery	.06
Other conversion costs	.23
Mill cost	.97
Cost plus 30% pretax	$1.42

8.1.1 Corn Versus Fossil Materials Prices Historic costs for various feedstocks over the decade of the Middle East oil crisis are shown in figure 9. Each is shown on a common basis of cents per pound as well as the more usual units for each. As can be noted, the costs for all fossil materials—gas, oil, and ethylene derived from these—rose at a very sharp rate over the 1970's. On the other hand, corn escalated at a much lower rate, and this is the basis for any hope of switching from petro materials to renewable materials.

Commercial acceptance of enhanced fermentation processes will ultimately depend on the direction taken by crude oil prices. What's going to happen in the future? The recession of the early 1980's, the Persian Gulf War, and the recession of the early 1990's really threw everyone's timetable out of date. The market is again soft at about $17-$20 per barrel. However, James McNabb of Conoco [58] has pointed out that OPEC operated at only 60% of capacity over the late 1980's. In the 1990's production is expected to reach 80%; and market power will shift back from the buyer to the seller, with a corollary increase in oil prices. At that time it is expected that the United States will be importing half of its oil supply instead of the 7% it imported at the time of the 1973 oil crisis. As a result he forecasts that oil prices will reach the mid

$30's by 1995 and $59 per barrel by the year 2000 (fig. 2). Other market watchers are also foretelling the start of the turnaround in oil prices in the near future (59-64).

What's going to happen to corn in the meantime? Some of the forecasts made by the USDA and industry sources suggest that corn prices will rise much more slowly than oil prices; from a low of $2.50 per bushel for the 1981-82 crop year to about $4.60 per bushel by the year 2000—a rise of about 3.4% per year.

8.1.2 Corn Sugar Cost Estimate The techno-economic studies to be discussed later were based on the availability of a contract supply of dilute 45% corn syrup from an adjoining wet mill at a transfer price of $0.065 per pound of equivalent glucose. The estimate was made by the author as an approximate, if not qualified, evaluation of substrate costs. It is shown in Table 24. The basis was for an early 1980 plant processing 60,000 daily bushels to produce 720 million annual pounds of syrup (dry basis). The wet mill yield was assumed to be 31.6 pounds of starch per bushel. Investment in the wet mill was estimated to be $40 million.

Table 24

COST ESTIMATE
OVER-THE-FENCE TRANSFER OF 45% CORN SYRUP

	$/lb Glucose
Corn @ $2.60/bushel	$0.074
Co-product Credits	
Corn Oil 1.7 lb/bu @ $0.26/lb	($0.013)
60% Gluten Meal 2.2 lb/bu @ $265/ton	($0.008)
Gluten Feed 11.5 lb/bu @ $125/ton	($0.020)
Total Credits	($0.041)
Net Corn	$0.033
Enzymes	$0.006
Labor	$0.007
Utilities	$0.008
Maintenance, Taxes & Insurance	$0.004
Depreciation	$0.004
Cost of Manufacture	$0.062
Selling, Administration & Research	$0.002
Earnings Before Taxes	$0.017
Selling Price	$0.081
Savings for contract 45% syrup	
Steam 1.15 lb/lb	($0.006)
Labor	($0.001)
Maintenance & Depreciation	($0.001)
Selling, Administration & Research	($0.001)
Earnings Before Taxes	($0.007)
Adjusted Contract Price	$0.065

Unfortunately, such price information is considered proprietary by wet millers and is not forthcoming. However, a recent analysis of the feedstock costs for fermentation ethanol plants [65] showed that over the period 1Q81–2Q86 at an average price for #2 yellow corn ex Chicago of $2.86 per bushel the average price for corn net of by-product credits was $0.039 per pound of glucose. Similarly, over the period 2Q87–1Q88 the corresponding costs were $1.79 per bushel and $0.009 per pound of sugar.

A corn price of $2.60 per bushel appears to correspond to a sugar cost of about $0.081 per pound of starch according to the correlation of published data shown in figure 17.

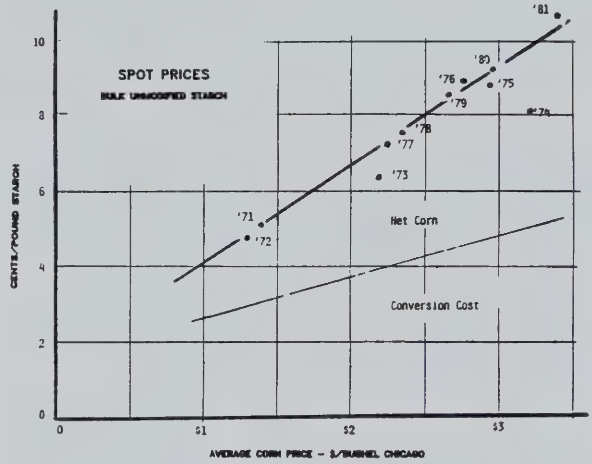


Figure 17

8.1.3 Hydrolysis of Polysaccharides If technically feasible the use of the polysaccharide directly would be economically preferred in most cases [66]. Programs at Massachusetts Institute of Technology and at the University of California at Berkeley were centered on this possibility.

However, most fermentations take place more readily using a monomeric sugar feedstock. Moreover it may be preferred in certain cases to have a large common supply of sugar feeding a number of smaller fermentation operations as part of a "biorefinery" complex.

The price of corn syrup puts a competitive ceiling on the market value of lignocellulose-based biosugars. In addition the residues from corn wet milling are high value oil and protein feeds, while markets for lignin and xylose, the residues from cellulose hydrolysis, have yet to be developed.

Cellulosic biomass at $25-$35 per dry ton is far cheaper than corn at $110 per dry ton [67,68]. However it is very difficult to hydrolyze cellulose because of the intractable nature of the cellulose crystallite. As a result, a trade-off occurs in a cellulose hydrolysis process between low raw material costs and higher investment for hydrolysis equipment as compared with a starch hydrolysis process.

Various pretreatment processes have been under study to improve hydrolyzability of cellulose. For example in the mild acid pretreatment process, wood chips or other sources of lignocellulose are acidified to hydrolyze and recover the hemicellulose sugars while opening up the structure of the alpha cellulose to enzyme attack [69]. The cost of the pretreatment, however, increases the cost of the wood chips from $35 per dry ton to over $90 per dry ton, as shown in Table 25. This means that a lot of the cost margin between wood and corn is lost.

Table 25

Pretreated Wood Chips
($/Dry Ton)

	1980	1985	1990
Hardwood Chips (40 Mile Haul)	$25.75	$36.80	$51.54
Cost Plus 30% PTROI – $/Dry Ton			
– Chips	$28.36	$40.48	$56.69
– Receiving & Grinding	6.70	9.92	14.42
– Acid Pretreatment	26.66	48.64	74.00
– Total	$61.72	$99.04	$145.11
¢/lb. Equiv. Sugar*	4.4¢	7.1¢	10.4¢

*at 90% Molar Yield of Polysaccharides (70% d.b.)

At present cellulose hydrolysis does not appear to be economically competitive with starch hydrolysis as a source of sugar. Processes using concentrated acids to catalyze the hydrolysis have been commercially unsuccessful because of the need to recover and recycle the acid. Dilute acid processes reduce acid-associated costs, but yields are poor, and they require rigid control of residence time at high temperatures. Consequently, power costs and investment are too high for these processes to compete with corn hydrolysis.

8.1.3.1 Concentrated Acid Hydrolysis The acid hydrolysis of cellulose is hardly new. Bergius' Reinau Process was based on the use of supersaturated hydrochloric acid as described in a German Patent No. 11836, issued in 1880. The process was operated up to the end of World War II.

Concentrated sulfuric acid was the basis for the process piloted by the USDA's Northern Regional Research Laboratory in 1945 [26] and by the Japanese at Hokkaido in the 1950's [81]. Neither process was commercialized because of the problem of recovering and recycling the acid.

Research on new versions of concentrated acid hydrolysis has lagged behind that on dilute acid processes. Michigan State University has made progress in using gaseous or liquid hydrogen fluoride at low temperatures to break down alpha-cellulose without subsequently degrading the sugars. However considerable reversion of the monomeric sugars to the oligomers occurs while increasing temperature to recover the HF. This requires a mild post-hydrolysis of oligomers by dilute sulfuric acid. The effect of this is to approximately equate process investment to that for the two-stage dilute acid process [70].

Other concentrated acid processes do not seem to be as firmly developed. This includes Purdue University's use of methanol to extract and recycle concentrated sulfuric acid from the acid-impregnated biomass residue [35]; and North Carolina State University's evaluation of superconcentrated 15N hydrochloric acid in a variation of the Bergius Process [36].

8.1.3.2 Dilute Acid Hydrolysis The use of dilute sulfuric acid was introduced by Scholler in a plant at Tornesch, Germany, in the 1930's [28]. This batch process used less acid but yields were poorer than with the concentrated acid processes. During World War II, the American War Production Board assigned further development of the process as a source of a feedstock for ethyl alcohol to the USDA's Forest Products Laboratory. The continuous "Madison" process that resulted was incorporated in a pilot plant built by the TVA at Wilson Dam [29] and in a larger plant built at Springfield, Oregon, that processed 300 tons of wood waste daily [30]. None of the dilute acid hydrolysis plants survived peacetime economies except for plants that continue to operate in the USSR [71].

Interest in acid hydrolysis as a route to alternative energy sources revived in the 1970's as a result of the world oil situation. Dilute 0.4 wt% sulfuric acid is being used at moderate temperatures, for example, 170 C/5 minutes as a mild prehydrolysis pretreatment for recovering heat sensitive hemicellulose sugars prior to applying the higher temperatures, e.g., 270 C/5 seconds, needed for hydrolyzing the crystalline cellulose. The two-step process has been explored at small scale in a number of laboratories, notably by USDA's Forest Products Laboratory [72] and by Dartmouth

College [73]. New York University had an advanced pilot system operating that used a Werner-Pfleiderer twin-screw extruder/reactor to control temperature and residence time to the limits critical to the yields of this process [74]. Georgia Institute of Technology and TVA had designed integrated pilot plants that were also based on dilute acid technology [75].

8.1.3.3 Enzymatic Cellulose Hydrolysis A biological approach to cellulose hydrolysis involves the use of cellulolytic enzymes such as those produced by the fungus: *Trichoderma reesei* [37]. This process had been under development by the U.S. Army Natick Laboratory since World War II. After the 1973 oil crisis at least 15 other laboratories around the world initiated similar projects. The enzyme is produced exocellularly in a separate fermentation process and transferred to the hydrolysis section as a supernatant liquid after filtering off the cells. Development of hypercellulolytic mutants at Natick Laboratories, Rutgers, and the Cetus Corporation increased the productivity in this step ten-fold to over 150 IU enzyme/L*hr [38,39].

Two problems remain: (1) the need to pretreat the cellulose feed to improve accessibility of the substrate to enzyme attack and (2) inhibition of the enzyme by the product glucose and its dimer, cellobiose.

Dartmouth College has shown that dilute acid prehydrolysis is an effective pretreatment [69,76], but this step adds $0.03 per pound to the cost of the sugar produced (1980 dollars). The Iotech [77] and Stake [78] steam explosion pretreatments and the Colorado State University/Texas A&M [79] liquid ammonia freeze-explosion technique may prove to be more cost effective. Clearly, however, there is still room for innovation in the area of activating crystalline cellulose to hydrolysis.

8.1.3.4 Hydrolysis Economics The economics of some of these hydrolysis processes are compared in Table 26. Even at best these approaches appear to provide only a trade-off between these untried new sources of glucose and corn syrup, a well established source. The dilute acid process reduces acid-associated costs compared with the concentrated acid process to about $0.003 per pound of sugar produced at a lignocellulose cost of $0.03 per pound of sugar (1985 dollars). However power costs are high. Plant investment amounts to $0.18 per annual pound, which is also too high for the process to compete in its present form with corn starch hydrolysis. Few in industry would become seriously interested in introducing such new processes unless a considerable apparent cost saving could be developed to justify the risk involved.

Table 26

Biomass costs (¢/dry lb.)

	1980	1985	1990
Corn Stover	1.5¢	2.1¢	3.1¢
Whole tree wood chips	1.3	1.8	2.6
Pre-treated wood chips *	4.4	7.1	10.4
Biosugar ex lignocellulosics			
Enzyme/acid pretreat	8.0	12.9	19.3
Concentrated acid/recycle	8.1	12.3	18.1
Dilute acid/extrusion	8.8	14.0	20.9
Concentrated acid/once-thru	12.6	18.7	26.8

* ¢/lb. equivalent biosugar

8.2 Conversion Costs

Conversion costs are the complement to the cost of raw materials making up the cost of manufacture. This usually includes labor-related costs, utility costs, and capital-related costs such as maintenance, property taxes and insurance and depreciation. Capital costs also must include some notion of return on investment anticipated by the company before electing to enter a new business. Hence, the capital cost for direct plant investment, allocated utility investment, and working capital is usually a dominant factor affecting total cost.

It is rather difficult to generalize about conversion cost differences between fermentation and petrochemical processes. Synthetic processes are usually operated in a continuous mode at large scale in order to attain the economics associated with such large scale operations. Heretofore, fermenters are more often operated in a batch mode. Although fermenters are relatively cheap per unit volume compared with high pressure synthesis reactors, large volumes are usually needed and fermentation plants are operated in multiple units. As a result as design capacity increases, the attendant decrease in investment per unit of production flattens out at a relatively low scale.

Similarly, although fermenters operate at low temperatures and low energy demands, the crude product is generally contained in a very dilute aqueous beer. As a result, product recovery operations can involve some very high energy and capital intensive processes such as distillation.

Innovations in both the fermentation system and in product recovery are sorely needed and could become rewarding areas for further research.

8.2.1 Fermentation Cost Of all the fermentation parameters, product concentration has the greatest effect on conversion cost. Batch time, or dilution rate for continuous operation, is second in importance. The effect of each on cost is shown in figure 18. Concentration is of primary importance because its reciprocal (gallons per pound of product) is a measure of the size of both the fermentation and recovery/purification plants needed to produce a unit of product. Dilution rate affects only fermenter volume. But since fermenter investment is usually a large proportion of total plant investment, the effect on cost can also be large. The chart shows the importance of increasing concentration above 100 g/l. This level is seldom realized in practice as a result of product inhibition of the organism—a problem very high on the list of economically relevant research priorities.

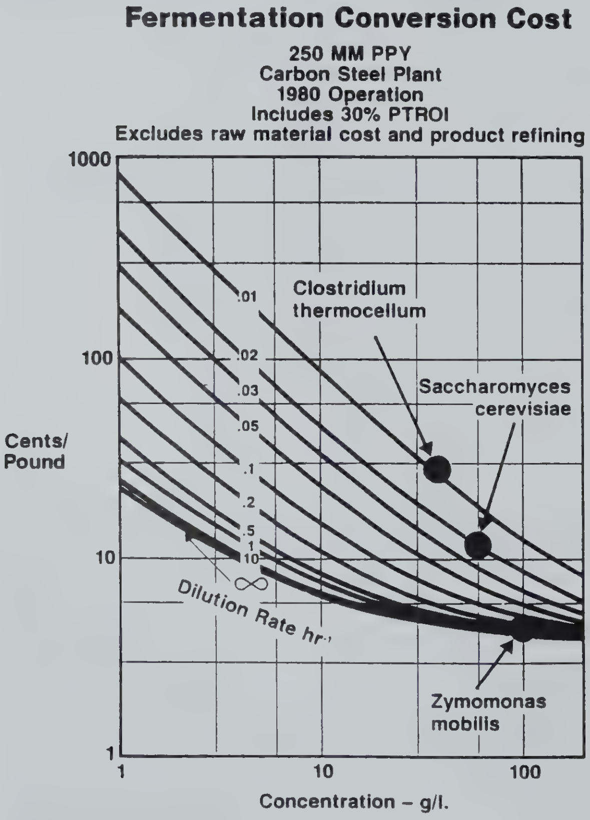


Figure 18

Likewise the advantage of continuous operation is evident. A batch mode requires about 12 hours to turn a large fermenter around at the end of the run. This means that even with a hypothetical zero fermentation time for the batch, the effective "dilution rate" would reach a maximum of 0.08 hr^{-1} (i.e., the reciprocal of 12 hours total cycle time). The convergence of the curves at an "infinite" dilution rate simply means that at high rates the effect of fermenter investment becomes of lesser importance than other investment items.

The conversion cost for three alternative routes to ethanol are compared on figure 18. The $0.12 per pound ($0.75 per gallon) cost for the *Saccharomyces cerevisiae* yeast system represents the conventional batch fermentation of corn sugar in a distillery [80] at a batch time of 54 hours and for a product concentration of 60 g/l as limited by product inhibition [46,47]. A more efficient system on corn sugar based on the bacterium *Zymomonas mobilis* [48] operates at a higher 100 g/l concentration as a result of lower product inhibition and at a higher effective dilution rate of 0.7 hr^{-1}. These two improvements reduce conversion cost to $0.05 per pound ($0.28 per gallon). In contrast to these two corn-based processed, MIT has been developing a process using the thermophilic bacterium *Clostridium thermocellum* to convert lignocellulosics directly to a mixture of 32 g/l ethanol plus 7 g/l acetic acid at a total batch time of 100 hours [81]. The longer time and lower concentration results in a higher $0.29 per pound ($1.80 per gallon) conversion cost. In this case, since the raw material cost is lower than for the corn-based processes, conversion cost can be higher and still effect a break-even position.

8.2.2 Product Recovery Costs In addition to the need to improve the fermentation process, a corollary need exists for new energy efficient processes to recover the products from dilute aqueous solution.

Recovering products from fermentation broths invariably involves separating the product from a dilute, usually under 10 wt%, more generally 1-5 wt% aqueous solution. The magnitude of this problem and the approach taken to solve it depends on whether the product has a boiling point below or above that of water, occurs as a salt or is a precipitate. Low-boiling organic solvents are relatively easy to separate from water by distillation as a result of usually high boiling point and volatility differences. Distillation is the present separation method of choice in these cases, particularly where the heat can be supplied by low pressure steam, and refrigeration is not required to condense the overhead vapors [82]. Since the solvent is boiled away from water, the energy expended is a simple function of its latent heat of vaporization; e.g., about 2300 Btu per gallon for ethanol [83]. As shown in figure 19, the heat lost to water is mainly that required in sensible heat to heat water to its boiling point. About 70% of this can be recovered by heat exchange with the feed. For a 5% ethanol broth leaving the fermenter at 35 °C, this heat amounts to about 14000 Btu per gallon or 2,220 Btu per pound of ethanol produced. In contrast, to recover a high-boiling product like acetic acid from water by distillation, the water must be boiled away from the product. In the case of a 5 wt% solution of acetic acid in water, this heat energy amounts to at least nineteen times the latent heat of water, or about 21000 Btu per pound of acid.

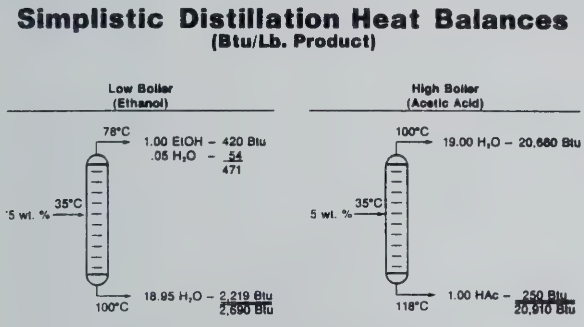


Figure 19

8.2.2.1 Low-Boiling Solvents Ethanol serves as a good example of a low-boiling solvent of current national interest. It also exhibits a minimum-boiling azeotrope with water. In the actual recovery of ethanol from fermentation broths, considerably more energy is required than indicated in the above simplistic example as a result of a need for a high reflux ratio to reach concentrations approaching the 95% azeotrope in the "pinch" region of the vapor-liquid equilibrium diagram. Indeed, outmoded beverage alcohol plants have reported overall process energy needs as high as 150,000 Btu per gallon [84].

Over recent years, a great deal of attention has been given to improving the recovery of anhydrous ethanol for use in gasohol. In newer, energy-efficient fermentation plants, total plant energy demand has been reduced to as low as 30000-50000 Btu per gallon. Most of this is for the recovery operation [85-93].

Various other recovery methods are also being introduced, including: vapor recompression distillation, multiple-effect distillation, supercritical extraction, azeotropic distillation, vacuum distillation, and sorption [94]. A summary for the energy demands for some such processes for recovering low-boilers is shown in Table 27. Some form of distillation combined with vapor recompression or cascaded pressure staging appears to be the current method of choice for producing product at concentrations up to the azeotrope. Such systems have been amply demonstrated in commercial practice. Each new case, however, should be evaluated on its own merit. The energy-saving adaptations require additional heat exchangers, compressors, etc., compared with conventional distillation. In some cases, particularly for small plants, adding such investment may not be justified by the value of the energy saved.

Table 27

Energy Demands for Recovering Ethanol from Aqueous Solution

Process	Concentration – Wt. % Initial	Concentration – Wt. % Final	Energy Form	Energy Demand – Btu/Gal. Actual	Energy Demand – Btu/Gal. Equiv. Steam*
Simple Distillation	10%	95%	Steam	18,000	18,000
Multiple Effect Distillation	10	95	Steam	7-10,000	7-10,000
Supercritical Extraction	10	91	Electricity	2,850	8,600
Vapor Recompression Distillation	10	95	Electricity	1,930	5,800
Azeotropic Distillation	95%	100%	Steam	9,400	9,400
Adsorption – Water	95	100	Steam	2,000	2,000
Vacuum Dehydration	10%	100%	Steam	37,000	37,000
Adsorption – Ethanol	10	100	Elect. & Steam	13,000	31,300
Simple Dist. & Azeo. Distillation	10	100	Steam	27,400	27,400
Vapor Recomp. Dist. & Adsorption	10	100	Elect. & Steam	3,930	7,800

*at 33% Steam-to-Electricity Conversion Efficiency

If anhydrous alcohol is needed, the new sorption processes for removing water from the azeotrope might be considered over the incumbent azeotropic distillation process. Appraisal of these processes as well as other new approaches, such as supercritical extraction, at pilot and demonstration levels should be continued.

8.2.2.2 High-Boiling Compounds As indicated earlier, the cost of distilling water away from a dilute higher-boiling product is prohibitively expensive. For example, acetic acid and water are relatively close in relative volatility. To recover glacial acid from a 1.5 wt% aqueous solution by simple distillation, as shown in figure 20, would require a column operated at a very high reflux ratio (2.8 L/D), at a steam load of 275,000 Btu per pound of acid recovered [95]. Hence, some other approach such as solvent extraction needs to be considered in this case.

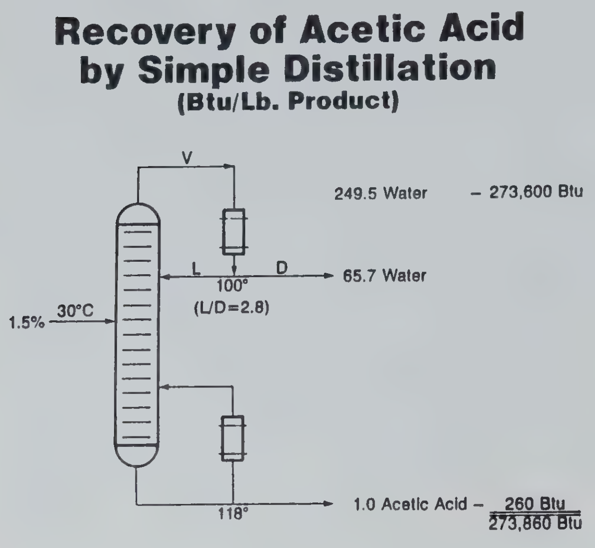


Figure 20

Solvent extraction combined with azeotropic distillation has been used for many years to recover dilute acetic acid in manufacturing cellulose acetate, vinyl acetate, and other products [96,97].

Acetic acid can be produced from glucose either directly using *Clostridium thermoaceticum* or indirectly by way of ethanol by the older two-step vinegar process using Acerobacter aceti or Acetobacter suboxydans [98]. In either case, if extraction were to be used to recover the product, the process would have to be operated at low pH to provide product as an extractable free acid rather than an unextractable salt. The acid could then be recovered by the extraction process shown in figure 21. For a plant scaled to produce 250 million annual pounds of glacial acetic acid, the direct investment in the recovery section for a grass-roots plant built at a midpoint of construction at mid-1982 would amount to $57 million. Product recover costs are shown in figure 21. Potential reductions in cost could be realized with increases in crude product concentration. The concentrations shown range from the low 10-20 g/l concentrations expected for the Clostridium thermoaceticum system [53] to the 55-120 g/l concentrations demonstrated by Wang for the Acetobacter suboxydans system on ethanol [51].

The energy demands for recovering acetic acid by various processes are summarized in Table 28. At the moment, solvent extraction appears to be the process of proven choice. Recovering free acid from salt solutions is much more difficult. To this end the continued development of the electrodialysis process is recommended. Membranes having improved structural integrity and antifouling characteristics need to be developed in parallel to the development of the process itself.

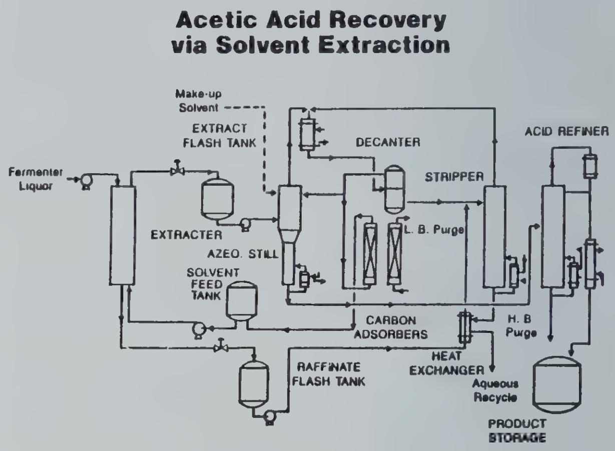


Figure 21

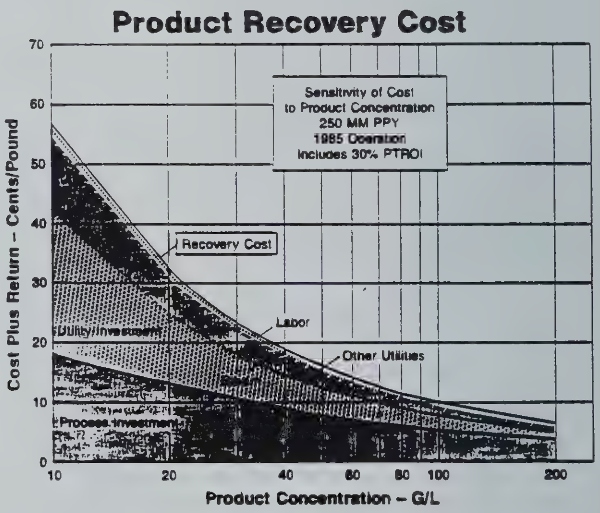


Figure 22

In summary, of the commercially demonstrated recovery processes, distillation appears to be most suited for low boilers, while solvent extraction appears well suited for high boilers. A number of new approaches, such as supercritical extraction, molecular sieve adsorption, and membrane separation hold promise for further development.

Table 28

Energy Demands for Recovering Acetic Acid from Aqueous Solution

Process	Feed Form	Concentration – Wt. %		Energy Form	Energy Demand – Btu/Lb.	
		Initial	Final		Actual	Equiv. Steam*
Simple Distillation	Acid	1.5%	100%	Steam	274,000	274,000
Melt Crystallization	Acid	1.0	100	Electricity	7,500	22,000
Solvent Extraction	Acid	2.0	100	Steam	31,200	11,000
Acidification/Extraction	Salt	1.5%	100%	Elec. & Steam	57,800	79,400
Vapor Recompression Evaporation	Salt	1.0	55	Electricity	10,400	31,200
Electrodialysis	Salt	1.0	100	Electricity	2,400	7,200

*at 33% Steam-to-Electricity Conversion Efficiency

9. CONCLUSIONS AS TO PROCESS NEEDS

Beginning in 1977, it became cheaper for the first time in 27 years to produce ethanol from corn instead of ethylene. Notwithstanding the current softness in the crude oil market, as the cost of petroleum rises again, it can be expected that at some future time the fermentation of renewable materials to produce other chemical feedstocks or specialty chemicals will become viable once again.

Prospects for biomass commodity chemicals are currently unfavorable as a result of: (1) generic deficiencies in the fermentation process, particularly with respect to generally low (below 5%) product concentrations and slow fermentation rates, and (2) lack of a present competitive advantage for renewable materials compared with depressed prices for crude oil [15,67,68,87,90,92]. However, research can alter the first limitation and Middle East politics, the second.

In the meantime, a national research program on biomass conversion is strongly urged as a strategic insurance policy to protect the American organic chemicals industry against further disruptions in crude oil supplies. Research should certainly feature fermentation programs. The concomitant development of both new fermentation systems and new recovery processes appears critical to restoring interest in the revitalization of a cost-competitive fermentation industry.

Concomitant research on lignin hydrogenation is also suggested as a means to broaden the potential bioproduct line.

In the following sections the technoeconomic position of several conceptual processes will be explored as to avenues for cost-effective research programs.

PART IV

Economic Potential of Recombinant Aerobes For Producing Specialty Chemicals

1. Introduction

The transfer of oxygen to aerobic cells has been a central focus of biochemical engineering since the advent of aseptic submerged fermentation in the mid-1940's. A central problem in the aerobic growth of any cell culture has been to maintain dissolved oxygen concentrations above growth-limiting levels, especially in high cell density fermentations. Productivity is often limited by the rate at which cells can aerobically catabolize the carbon source. Oxygen limitations frequently result in generation of growth-limiting metabolites [1,2].

The transfer process basically involves two sequential steps: (1) the transfer of oxygen from the gas phase into the liquid phase at a sufficiently high rate so as to maintain the dissolved oxygen concentration at an optimal level for (2) assimilation by the organism at its maximum biological limit.

All previous strategies for improving oxygen transfer have concentrated on improving the delivery of oxygen from air or oxygen gas to the surface of the cell by manipulating various environmental parameters of the fermenter medium.

In contrast an alternative genetic strategy was recently developed for improving the cellular utilization of oxygen and, possibly, also altering aerobic metabolism control under a less than optimum oxygen environment in the liquid phase [3,4,5]. This approach involves isolating the gene for a novel hemoglobin molecule, which is expressed by the aerobic bacterium *Vitreoscilla* in poorly oxygenated environments, and expressing it in *Escherichia coli*. The recombinant cells contain heme as well as active hemoglobin and grow faster and to considerably greater cell densities than comparable plasmid-containing cells that do not express hemoglobin.

The genetic approach is in a very early research stage, with little known about the specific potential for process improvement. Consequently it was the objective of this study to evaluate various aerobic fermentation systems of commercial importance to identify process shortcomings of economic significance that might be overcome by applying the genetic approach, or indeed, improved physical aeration approaches; and as a result direct this research along economically relevant pathways. The processes chosen for the analysis were those for producing bovine growth hormone, a functional cloned protein product, glutamic acid, and citric acid. Each of these is illustrative of a broad range of pharmaceuticals or chemical specialties produced over a wide range of plant capacities.

2. Mechanical Aeration

As noted by Hubbard [6], maintaining the dissolved oxygen content at an optimal value in the fermenter broth is usually the limiting factor in the design of an aeration system for an aerobic fermentation. This usually translates into providing sufficient energy in the form of agitator shaft horsepower and/or compressed air to a sparger so as to provide small air bubbles having a high surface/volume ratio and, consequently having a high rate of diffusion between the gas and liquid phase.

Since it was not the intention of this study to evaluate the effects of mechanical aeration strategies on economics, power requirements for the economic models were set at a level of 3.4 HP/M^3. From a brief review of the literature, this appeared adequate to insure sufficient oxygen transfer within the broth to provide for the needs of the organism [7-12].

3. The Biocatalyst Approach

The genetic approach is based on cloning into the production strain of interest a functional gene encoding the hemoglobin of the bacterium *Vitreoscilla*. The strategy has been demonstrated to date in *E. coli*, in which functional *Vitreoscilla* hemoglobin has been expressed after inserting the hemoglobin gene on a multicopy plasmid [3]. *E. coli* cells containing hemoglobin respire more rapidly than plasmid-containing controls, especially under microaerobic conditions. Similarly, *E. coli* containing hemoglobin grow substantially more rapidly and attain higher cell densities under oxygen-limited conditions than control strains which do not synthesize hemoglobin [4,5]. Preliminary data also suggests that the presence of hemoglobin reduces acetate production under microaerobic conditions.

Implementation of this strategy in other industrial aerobic organisms is now in progress. *Vitreoscilla* hemoglobin has been successfully expressed in one type of eucaryotic cell, suggesting that there are no fundamental barriers to applying this strategy to many different types of aerobic bioprocesses.

4. Expected Impact of Recombinant Aerobes

The final concentration achieved in an aerobic bioprocess is often directly correlated to the maximum achievable biomass. Maximum biomass concentration is in turn often limited by oxygen supply to the system. Because cloned hemoglobin has been demonstrated to enhance respiration and growth under oxygen-limiting conditions and to enable growth to higher cell densities in laboratory situations, it is expected that this technology will enable fermentation operations to attain higher cell densities in batch and fed-batch processes and to enhance cell recycle in continuous processes. A second benefit of extending the duration of culture activity will be to increase the length of the batch operating cycle at a time when volumetric productivity is greatest.

There is insufficient data at present to estimate accurately how much cell density can be increased using this technology. In shake flask and fed-batch fermentations, cell density increases of 50% to almost 100% have been observed as a result of the presence of cloned hemoglobin. However, these cultures were not grown in an optimized fashion to reach maximum attainable cell densities in the control.

Exploratory experiments in the laboratory have also indicated that increased specific growth rates can be provided by the presence of cloned *Vitreoscilla* hemoglobin. The possibility that acetate formation might be reduced in fed-batch fermentations would also enable more rapid feeding of the culture with accordingly higher growth rates. In a continuous process this behavior would permit a higher dilution rate.

One objective of further research on recombinant aerobes is to define the magnitude of potential improvements to the fermentation systems. This economic analysis was carried out with the aim of guiding this research.

5. Products Selected For Study

Processes for producing bovine growth hormone (BGH), a cloned protein, glutamic acid, and citric acid were selected as the evaluation "vehicles" because they represented a broad range in plant production scale for specialty chemicals and also allowed a comparison between endogenous protein products and exogenous chemical products.

The BGH process, and the conclusions drawn thereon in this study, might also serve as a crude model for the production of a great number of biologically active drugs such a interferon, human insulin, interleukin II, etc., with due regard for the effects of production scale on cost.

The cloned protein product category is actually an extension of the BGH model to a production scale of 1 million annual pounds to represent other protein products in this production volume category.

The production of glutamic acid in its preferred form as the flavor enhancer, monosodium glutamate monohydrate, outstrips all other amino acids in world volume (860 million pounds) and value ($750 million) [13]. Citric acid is a specialty chemical bordering on a commodity chemical in production volume (235 million pounds valued at $191 million) [14].

6. Basecase Conditions for Process Models

Process operating data for the models were obtained from the literature [11][15-23]. The basecase conditions are summarized in Table 29.

A batch mode was assumed in all basecases, although the economic potential for continuous operation coupled with cell recycle was evaluated for the exogenous chemicals. For the proteins a common stage was used for concurrent cell growth and product expression. The models for the chemicals assumed that cell growth and product formation could occur in either common or sequential stages.

It is hoped that the basecase conditions represent the state of the art. Realistically, however, it is recognized that up-to-date proprietary process information is seldom available from producers. Accordingly the cost estimates may err on the high side, although the conclusions to be drawn are still believed to be valid.

Table 29

Aerobic Fermentation Performance Batch Fermenter Cases

	Bovine growth hormone	Cloned protein	Glutamic acid	Citric acid
Production level, million PPY	0.02	1.0	25.0	50.0
Fermenter mode	Batch	Batch	Batch	Batch
Growth/production stages	Common	Common	Sequential	Sequential
Product concentration, g/L	7	7	90	90
Cell density, g/L	42	42	18	8
Specific productivity, g/g cells · h	0.007	0.007	0.18	0.24
Fermentation yield, % of glucose converted	5	5	54	89
Recovery yield, % of product in broth	60	60	98	98
Batch cycle, h				
Growth	24	24	6	24
Production			29	46
Turnaround	3.5	8	12	12
Volumetric productivity, g/L · h	0.25	0.22	2.2	1.6
Production fermenters, gallons	3 × 1000	3 × 60,000	3 × 100,000	6 × 130,000
Fermentation power, HP/1000 L	3.4	3.4	3.4	3.4
Aeration ratio, 02 fed/transferred	3:1	3:1	3:1	3:1
Oxygen transferred, mM/L · h	14	14	55	15

In addition to the large differences in production scale between the protein and chemical products, a number of other inherent process differences exist. The intracellular proteins have only low product concentrations; very low yields relative to substrate converted; very low yields across the recovery and refining operations; and are not amenable to the potential benefits of cell recycle as are the extracellular chemical products.

7. Basecase Economics

Basecase economics for the four processes were determined using technoeconomic models developed by Bio En-Gene-Er Associates, Inc. The time frame was a plant built at a Midwest site on the Mississippi River with a midpoint of construction in 1984, a start-up in 1986, and operating in 1988 at full production following two start-up learning years. Stainless steel fermenters were used in each case.

The analysis includes only the process steps common to all the processes, namely: raw materials receiving, medium preparation and sterilization, fermentation, beer/cell filtration, and final product storage. *Recovery and refining operations were not included in the analysis since these vary from process to process.*

A summary of product economics for the basecases is shown in Table 30. The cost factors used, were based on actual operating experience for a plant as described in the site scenario. Considering that recovery costs are not included, selling prices to earn a 30%-40% pretax return on investment appear reasonable compared with market prices as of February, 1989, of $0.86/lb for monosodium glutamate and $0.835/lb for anhydrous citric acid [24]. Bovine growth hormone has more of the attributes of an expensive pharmaceutical—which it is—rather than those of a chemical [25].

Table 30

Aerobic Fermentation Comparisons Batch Fermenter Basecases

		Bovine growth hormone	Cloned protein	Glutamic acid	Citric acid
Production level, Million PPY		0.020	1.0	25.0	50.0
Investment, $million (1984)					
Direct Permanent Investment (DPI)		$1.97	$8.8	$15.0	$32.7
Allocated Power, Service, & Gen'l (APS&G)		$0.21	$1.3	$2.6	$5.5
Working Capital		$0.69	$2.2	$2.8	$4.5
Total Investment (TI), $Million		$2.87	$12.3	$20.4	$42.7
, $/lb		$143.49	$12.29	$0.82	$0.85
Cost, $/lb (1988)					
Raw Materials					
Sugar Syrup	@$0.081/lb glucose	$2.56	$2.56	$0.129	$0.076
Nutrients	@Current prices	$0.47	$0.47	$0.016	$0.004
Total Raw Materials		$3.03	$3.03	$0.145	$0.080
Utilities					
Electricity	@$0.040/KWH	$0.32	$0.36	$0.027	$0.044
Steam	@$2.20/1000 lb	$0.02	$0.02	$0.001	$0.001
Cooling Water	@$0.040/1000 gal	$0.00	$0.01	$0.002	$0.002
Process Water	@$0.500/1000 gal	$0.01	$0.01	$0.001	$0.001
Biodegradation	@$0.040/lb dry solids	$0.11	$0.11	$0.001	$0.001
Total Utilities		$0.46	$0.51	$0.032	$0.049
Labor-Related					
Dir. Op. Wages & Benefits (DOW&B)	@$26.40/man-hour	$51.68	$1.55	$0.069	$0.042
Dir. Salaries & Benefits	@18% DOW&B	$9.30	$0.28	$0.012	$0.007
Op. Supplies & Services	@6% DOW&B	$3.10	$0.09	$0.004	$0.002
Gen. Plt. O'head on Operations	@23% DOW&B	$14.02	$0.42	$0.019	$0.011
Control Laboratory	@$19.22/man-hour	$30.26	$0.81	$0.016	0.008
Tech. Assistance to Mfg	@$22.06/man-hour	$0.00	$0.09	$0.002	$0.001
Total Labor-Related		$108.36	$3.24	$0.122	$0.071
Capital-Related					
Maint. Wages & Benefits (MW&B)	@1.7% DPI	$1.68	$0.15	$0.010	$0.011
Maint. Salaries & Benefits	@25% MW&B	$0.42	$0.04	$0.003	$0.003
Maint. Materials & Services	@40% MW&B	$0.67	$0.06	$0.004	$0.004
Maint. Overhead	@4% MW&B	$0.07	$0.01	$0.001	$0.001
Gen. Plt. O'head on Maintenance	@23% MW&B	$0.48	$0.04	$0.003	$0.003
Taxes & Insurance	@0.3% DPI	$0.30	$0.03	$0.002	$0.002
Depreciation on DPI	@8% DPI	$7.91	$0.70	$0.047	$0.052
Depreciation on APS&G	@6% APS&G	$0.62	$0.05	$0.006	$0.007
Total Capital-Related		$12.14	$1.11	$0.076	$0.083
Cost of Manufacture		$123.99	$7.89	$0.374	$0.282
Selling Expense	@6% Sales	$13.04	$0.39	$0.021	$0.019
Distribution	Varies	$2.00	$0.01	$0.010	$0.010
Research & Development	@6% Sales	$13.04	$0.59	$0.033	$0.029
Administrative Expense	@2% Sales	$4.34	$0.26	$0.014	$0.012
Incentive Compensation	@6% Earnings	$3.45	$0.22	0.014	$0.015
Cost of Sales		$159.86	$9.36	$0.466	$0.367
Pretax Earnings	@30%-40% TI	$57.45	$3.69	$0.241	$0.256
Cost-Plus-Return Selling Price		$217.31	$13.05	$0.707[a]	$0.623

[a] $0.60 as monosodium glutamate monohydrate

8. Effect of Production Scale

The relative importance of the major cost elements is indicated in Table 30 and figure 23. The production scale of bovine growth hormone is so low that economics are overwhelmed by the cost of labor—a cost element for which improvements in aeration hold little promise. Nevertheless, improvements in aeration leading to reductions in investment could result in large absolute reductions in capital charges even though the relative effect is overshadowed by high labor charges.

Among the cases studied, the contribution of labor to total cost decreases as production scale increases. In contrast, the importance of investment increases.

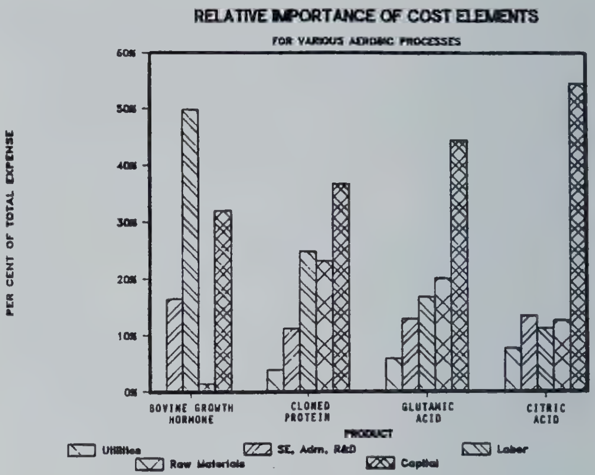


Figure 23

For the higher volume processes, capital-related costs (including earnings required for an acceptable return on investment) comprise the most important of the cost elements. Fermenter investment for the protein products is high relative to the chemical products for two reasons: (1) product concentration is low, and volumetric productivity is accordingly low and (2) for BGH the small 1000-gallon fermenters cost $500 per installed gross gallon compared with $20 per gross gallon for fermenters in the 150,000-gallon size. The relative position of capital-related charges for fermenter investment increases faster with increases in scale than other investment elements because at high production levels fermenters are added in multiples of large fermenter units and investment is less scale sensitive than investment for other equipment pieces (Table 31). Clearly, research on aeration should be concentrated on ways to reduce investment.

The cost of raw materials ranks a distant second to capital charges. High substrate demand and raw material cost are related to: (1) poor product stoichiometry, i.e., a low chemical yield for the metabolic pathway followed by the organism; (2) high cell growth relative to protein product formation; and (3) poor recovery of protein products across the recovery and refining steps. It does not appear that improvements in aeration effectiveness can help this situation. However this point needs to be explored more fully.

The effect of scale on the production of cloned proteins is shown in figure 24. A ten-fold increase in production rate results in a ten-fold increase in fermenter investment, but only a seven fold increase in total plant investment. Cost-plus-return is cut in half. In figure 24 as well as other figures in this report, the state-of-the-art basecase value is shown as a black dot.

Table 31

Distribution of Investment Among Process Elements

Process	Bovine growth hormone	Cloned protein	Glutamic acid	Citric acid
Production, Million PPY	0.020	1	25	50
Investment, $/annual lb				
Electric	$0.18	$0.21	$0.02	$0.03
Other allocations	$9.08	$0.98	$0.06	$0.07
Aeration	$1.24	$1.24	$0.10	$0.04
Prep, sep and storage	$17.15	$3.58	$0.21	$0.17
Fermenters	$70.55	$3.10	$0.23	$0.38
Total plant	$98.20	$9.11	$0.62	$0.69
Investment, % of total plant				
Electric	0.2%	2.3%	3.2%	4.3%
Other allocations	9.2%	10.8%	9.7%	10.1%
Aeration	1.3%	13.6%	16.1%	5.8%
Prep and storage	17.5%	39.3%	33.9%	24.6%
Fermenters	71.8%	34.0%	37.1%	55.1%
Total	100.0%	100.0%	100.0%	100.0%

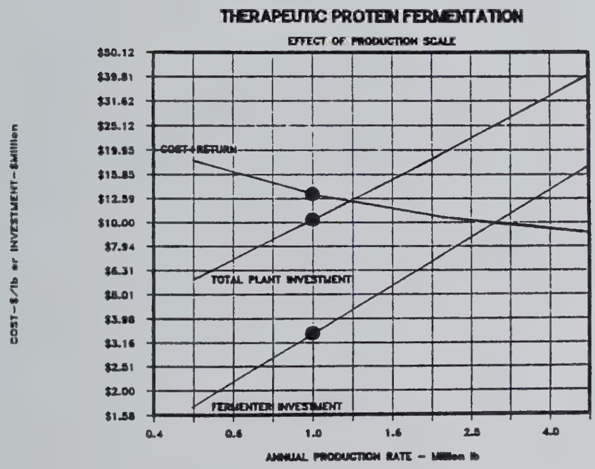


Figure 24

9. Effect of Product Concentration

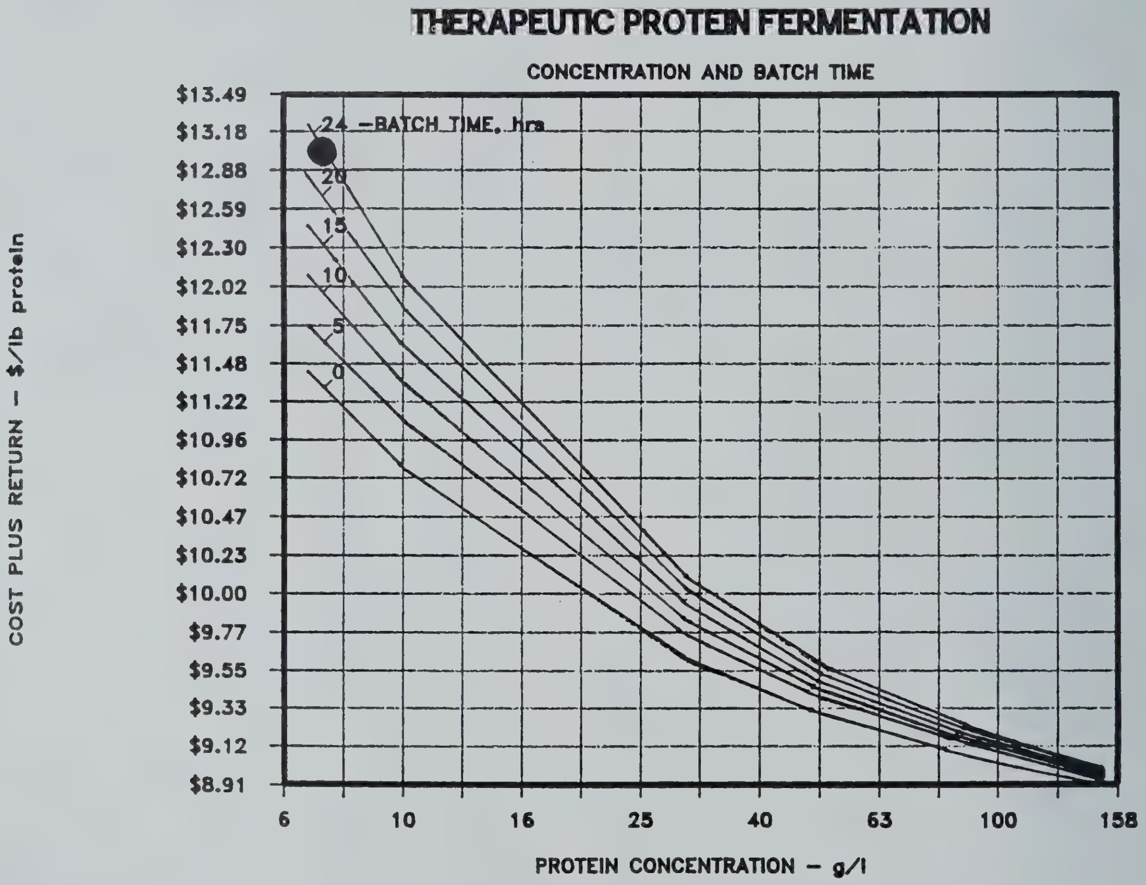
Product concentration is the most important of the process variables affecting investment and, hence, cost. Its reciprocal, liters of medium per gram of product, is an indicator of the volume and, hence, investment required for the entire plant at a desired level of production. Preferably, concentration should be increased at constant cell density and fermentation time. Provided product inhibition is not a factor, this can be accomplished at least theoretically by increasing specific productivity, g product/g cells*hr, or, in the case of exogenous products, by recycling cells to build density without adversely affecting yield. If product inhibition is a factor, a genetic change would have to be made to the organism to reduce sensitivity to product.

The effects of increasing product concentration are shown in figure 25 for a cloned protein and in figure 26 for glutamic acid. The data for BGH and citric acid are similar. In all cases, product cost drops rapidly at low product concentration in the 10-40 g/l range, but begins to level off at concentrations above 100 g/l showing the diminishing effect of the reciprocal of concentration at high concentrations.

10. Effect of Fermentation Time

Batch time, or its reciprocal, dilution rate, for a continuous process, is another important variable affecting investment. However, unlike product concentration which affects all investment, changes in time affect only the investment in fermenters. Nevertheless, since fermenter investment is usually a major part of total investment (see Table 31) time is accordingly important to cost.

From the above discussion of the effects of product concentration it appears that strategies for reducing time should not do so at the expense of concentration; for example developing a thermophilic organism having a lower product inhibition threshold. The interrelation of time and concentration is shown on figures 25 and 26. The effect of time is strongest at low product concentrations, but becomes increasingly insignificant at high concentrations where capital charges, and in particular, fermenter investment, become less significant elements of total cost. Note also that even at a zero batch time for the cloned protein case, cost is still quite high.


THERAPEUTIC PROTEIN FERMENTATION

CONCENTRATION AND BATCH TIME

Figure 25

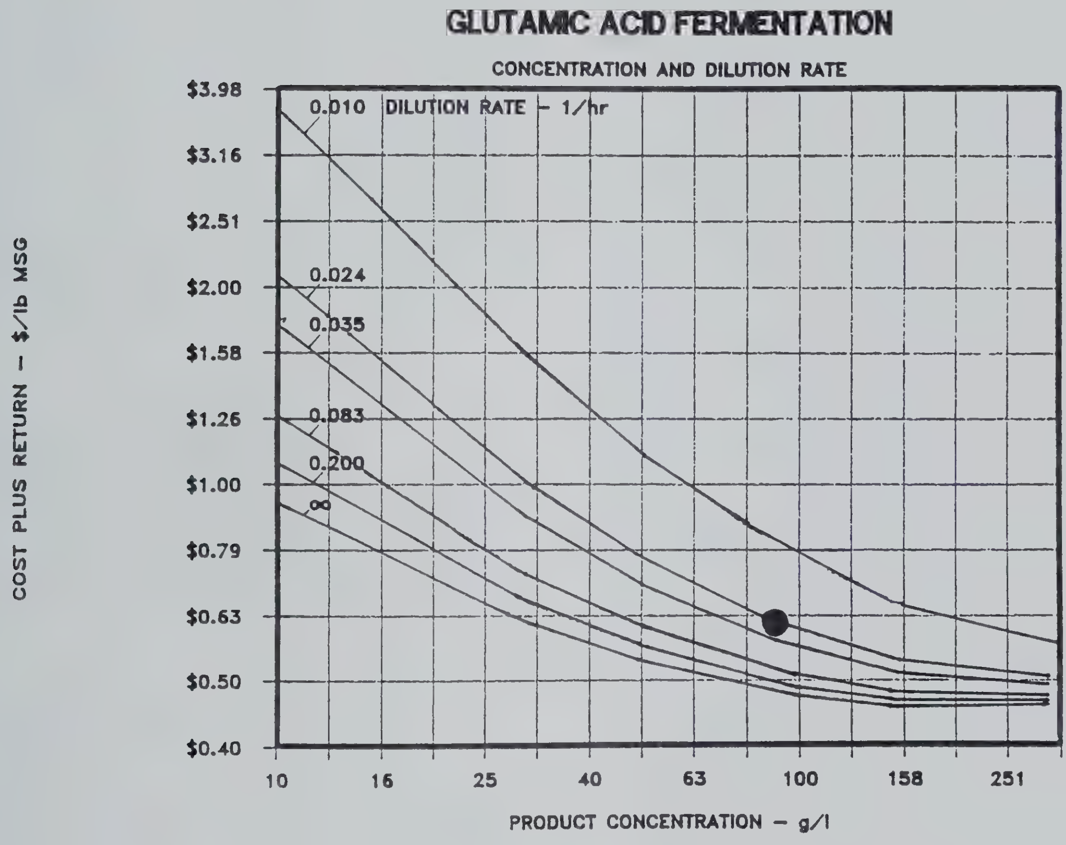

GLUTAMIC ACID FERMENTATION
CONCENTRATION AND DILUTION RATE
0.010
DILUTION RATE – 1/hr
0.024
0.035
0.083
0.200
∞
$3.98
$3.16
$2.51
$2.00
$1.58
$1.26
$1.00
$0.79
$0.63
$0.50
$0.40
COST PLUS RETURN – $/lb MSG
10
16
25
40
63
100
158
251
PRODUCT CONCENTRATION – g/l

Figure 26

11. Effect of Continuous Operation

The very real advantage of operating in a continuous mode in producing extracellular products is also illustrated in figure 26. In this plot, dilution rate is expressed as the reciprocal of time for continuous operation or as the reciprocal of batch time (bt) plus turnaround time (tt); i.e., 1/(bt + tt) for batch operation. For the large fermenters used in these models, a turnaround time of 12 hours was assumed in batch operation for emptying, cleaning, sterilizing, refilling and inoculating the fermenter for the next batch. None of this would be required for continuous operation over extended campaign periods. The maximum apparent dilution rate for a large batch fermenter at zero batch time would be 0.083 hr^{-1}, i.e., 1/12 hrs. The cost curve for that rate represents the floor of cost for the batch model. However, the cost for continuous fermentation could be reduced even lower to near the costs for "infinite" dilution rate. At or near that point the effect of fermenter investment on cost is not significant.

12. Effect of Specific Cell Productivity

In an endogenous batch process, the only way to reduce fermentation time and, as a result, fermenter investment, at the desired maximum product concentration attainable would be to increase the specific productivity of the cell. The effect of increasing specific productivity of intracellular systems is shown in Table 32 for BGH. As specific productivity is increased, volumetric productivity increases and batch time can be reduced accordingly. Fermenter investment (FI) is reduced as a result, and becomes an increasingly smaller part of total plant investment (TPI). Because of the flywheel effect of other cost elements, however, product cost does not drop in proportion to productivity.

13. Effect of Cell Recycle

Although exogenous product systems would also benefit from increases in specific productivity, the same effect could be obtained much easier by recycling cells to higher cell densities at constant specific productivity. This effect is shown in Table 33 for both batch and continuous production of citric acid. Both the glutamic acid and the citric acid fermentations reach high product concentrations. As noted earlier, this diminishes the relative effect of reductions in fermentation time. Recycling cells would have a greater effect on reducing costs for systems which are severely product inhibited. Nevertheless, product costs for the acid fermentations could be reduced 15-28% by recycling cells to high 150 g/l levels.

Such high levels may not be attainable as a result of the adverse effect of broth viscosity on aeration [26-30] unless recombinant aerobes can be developed to tolerate such microaeration environments.

Table 32

Bovine Growth Hormone Effect of Productivity on Fermentation Performance for 6.9 g/L Product Concentration

	For batch operation—3.5-h turnaround					
Specific productivity, g/g · h	Batch time, h	Volume productivity, g/L · h	Oxygen transfer, mM/L · h	Cost + return, $/lb	Ferm. invest., $MM	FI/TPI
0.0023	72.0	0.09	4.6	$317	$4.3	83%
0.0027	60.0	0.11	5.5	$292	$3.6	81%
0.0034	48.0	0.13	6.8	$267	$2.9	80%
0.0045	36.0	0.18	9.1	$242	$2.2	77%
0.0068	24.0	0.25	13.7	$217	$1.6	72%
0.0136	12.0	0.45	27.3	$192	$0.9	62%
0.0271	6.0	0.73	54.6	$180	$0.5	52%

Table 33

Citric Acid Manufacture Effect of Cell Recycling on Fermentation Performance for 90 g/L Product Concentration

	For batch operation—12-h turnaround					
Cell density, g/L	Batch time, h	Volume productivity, g/L · h	Oxygen transfer, mM/L · h	Cost + return, $/lb	Ferm. invest., $MM	FI/TPI
8.2	46.0	1.55	15	$0.62	$21.3	56%
15.0	25.2	2.42	28	$0.55	$15.9	50%
30.0	12.6	3.66	56	$0.50	$12.6	45%
50.0	7.5	4.60	93	$0.49	$11.3	42%
80.0	4.7	5.38	149	$0.48	$10.6	41%
110.0	3.4	5.83	205	$0.48	$10.3	40%
150.0	2.5	6.20	279	$0.48	$10.0	39%
	For continuous operation					
Cell density, g/L	Dilution rate, 1/h	Volume productivity, g/L · h	Oxygen transfer, mM/L · h	Cost + return, $/lb*	Ferm. invest., $MM	FI/TPI
8.2	0.02	1.96	15	$0.58	$18.2	53%
15.0	0.04	3.58	28	$0.50	$12.8	45%
30.0	0.08	7.16	56	$0.46	$9.5	39%
50.0	0.13	11.93	93	$0.44	$8.2	36%
80.0	0.21	19.08	149	$0.43	$7.5	34%
110.0	0.29	26.24	205	$0.42	$7.1	33%
150.0	0.40	35.78	279	$0.42	$6.9	32%

14. Conclusions and Recommendations

The transfer of the hemoglobin gene into aerobic organisms of commercial interest appears have merit from both a product expression as well as economic point of view. For systems such as those analyzed in this study, it is recommended that research on improved aerobes for product expression be directed toward developing properties that can lead primarily to a reduction in plant investment, with emphasis on reducing fermenter investment. Even for functional protein products to be produced at small scale, the cost of investment could be effectively reduced by advances in aeration. Although the relative savings might be masked by high labor charges, high absolute savings could result. Reducing investment might be accomplished by : (1) increasing product concentration; (2) reducing fermenter time and volume: (a) for extracellular products, by recycling cells to a higher density at constant specific productivity, or (b) for either extracellular or intracellular products, by increasing the specific productivity (g product/g cells*hour) of the cells; (3) converting to continuous operation.

PART V

Ethanol: The Ultimate Feedstock

Technoeconomic Evaluation of Ethanol Manufacture In Fluidized Bed Bioreactors Operating With Immobilized Cells

1. Introduction

The recent war in the Persian Gulf only accentuated the extent to which the United States in dependent on an uncertain oil supply. Even before this crisis many market forecasters were predicting an upswing in the price of crude oil [1-7]. Consequently, over the past decade a large number of research programs have been directed toward exploring the potential use of abundant renewable materials as basic feedstocks for ethanol.

Ultimately, ethanol will have to become one of the most important chemical feedstocks, if only because it can provide a technically demonstrated, albeit not yet economical, route to ethylene. Ethylene is the most important feedstock for the chemical industry. U.S. production amounted to 37.5 billion pounds in 1990 [8]. If ethanol could be produced at a low enough price to serve as the precursor to ethylene and butadiene, it and its derivatives could account for 159 billion pounds, or 50% of the U.S. production of 316 billion pounds of synthetic organic chemicals, presently valued at $113 billion [9]. This use would consume 4.2 billion bushels or about 54% of the 7930 bushel corn crop estimated by the USDA for the 1990/91 crop year [10].

Unfortunately, reaction stoichiometry is on the side of the petrochemical routes to ethylene. At a yield of 98%, it requires 1.64 pounds of ethanol to produce a pound of ethylene. As a result, raw material economics are adversely affected. It is enough at the moment to hope that the cost of fermentation ethanol can continue to compete with the cost of producing ethanol from ethylene.

2. Market Position

The United States leads among major world producers of industrial ethanol (11). (But not of fuel-grade ethanol, which is dominated by Brazil as a result of its support program for ethanol/gasoline blends). Production of synthetic ethanol has declined while fermentation ethanol has increased over the past decade.

Million Gallons	Synthetic	Fermentation	Total
United States	150	600	750
Western Europe	150	350	500
Japan	25	25	50

In the United States synthetic ethanol is produced in the Shell process by the direct hydration of ethylene. At a yield of 97%, it requires 0.63 pounds of ethylene per pound of ethylene. Over the decade prior to 1973 the price of ethylene and synthetic ethanol were relatively stable at $0.035 per pound and $0.35 per gallon respectively. However, soaring chemical prices resulting from the energy crisis of 1973 raised the price of ethylene to a peak of $0.26 in 1981. Following this it dropped back to $0.15 per pound before rising to the 2Q91 price of $0.24 or $1.00 per gallon of synthetic ethanol [12]. This cost is almost as much as the current $1.20 (depressed) price for fermentation ethanol.

3. Fuel Ethanol Plants of the 70's

The period of the late 1970's marked the heyday of construction of new fuel ethanol plants or retrofitting of former liquor distilleries. A case was developed for such a facility assuming a 60-million gallon yeast-based plant with a midpoint of construction of 1976 and operating in 1980. Cell recycle was not included. Thus the case was an attempt to reconstruct the economics for the plants that constituted the fuel alcohol industry at that time.

Investment in this plant in 1976 dollars amounted to $1.57 per annual gallon, comprising $1.31 for direct and allocated plant investment and $0.26 for working capital. Of the plant investment, the cost of twelve 500,000 gallon fermenters accounted for 46%.

The cost of manufacture (mill cost) amounted to $1.00 per gallon at a cost of sales of $1.26. This cost performance leads to a pretax return on investment of 30% for a selling price of $1.79 per gallon. Raw materials comprise 58% of cost of manufacture and 32% of selling price. Capital-related charges account for 37% of selling price.

This case is compared in Table 34 with several estimates made in about 1980 by various organizations: a task force of the American Institute of Chemical Engineers chaired by I. B. Margiloff of Publicker Industries [13]; a study commissioned by the Department of Energy [14]; and a study made by the Katzen organization for a plant with maximum energy recovery [15-17]. Agreement is generally good considering the diverse viewpoints and bases.

Table 34

COMPARISON OF ESTIMATES
ETHANOL PROCESS ECONOMICS
BATCH FERMENTATION - NO CELL RECYCLE

ESTIMATE		AIChE	D.O.E.	KATZEN	B.E.A.
CAPACITY - Million GPY		40	50	50	60
Mid-Point of Construction				1981	1976
INVESTMENT-$/gal					
Direct & Alloc. Plant Investment				$1.28	$1.31
Working Capital				0.12	0.26
Total Investment				$1.40	$1.57
COST-$/gal	Operating Year:	1980	1983	1983	1980
Corn		$1.12	$1.20	$1.09	
B.P. Credits		(0.50)	(0.60)	(0.47)	
Net Corn		$0.62	$0.60	$0.63	$0.56*
Other Raw Materials		0.14	0.07	0.02	0.01
Total Raw Materials		0.76	0.67	0.65	0.57
Utilities		0.19	0.20	0.11	0.22
Labor-Related		0.07	0.08	0.06	0.06
Capital-Related			0.17	0.21	0.15
		0.43			
Cost of Manufacture			$1.12	$1.03	$1.00
SE, D, R&D, Adm, & I.C.			0.18	0.18	0.26
Cost of Sales		$1.43	$1.30	$1.21	$1.26
Pretax Earnings @ 30% ROI				0.47	0.53
Selling Price				$1.68	$1.79

* Syrup ex wet mill at $0.038/lb equivalent glucose

4. Effect of Venture Timing

If the plants described in the preceding section were to be built today, costs would be substantially higher. Construction costs for a plant with a midpoint of construction of 1986 would be 79% higher than the plant built in 1976. Also, the cost assumed for substrate in 1988 was almost twice that used in the earlier estimate. This point is discussed later. As a net result the selling price in 1990 would have to be $2.58 per gallon to yield a 30% pretax return as compared with currently distressed prices of $1.20 per gallon for fuel alcohol [18]. This may be one reason why new plants are not being built.

The estimate for 1990 operation is compared with that for 1980 in Table 35. The effects of raw material and capital charges are clear. *The 1990 estimate serves as the basecase in this study for comparison with the estimates made for plants employing more advanced technology.*

Table 35

EFFECT OF VENTURE TIMING
60 MM GPY ETHANOL MANUFACTURE
INHIBITED SACCHAROMYCES YEAST
BATCH FERMENTATION - NO CELL RECYCLE

MID-POINT OF CONSTRUCTION	1976	1984
CONSTRUCTION COST INDEX	74	128
OPERATING YEAR	1980	1988
SUBSTRATE COST - $/lb equiv. glucose	$0.038	$0.065
INVESTMENT-$Million		
Direct Permanent Investment	$54.5	$91.1
Allocated Power, Services & Gen.	$24.1	$26.8
Working Capital	$15.4	$22.1
Total Investment	$94.1	$140.0
COST-$/gal		
Raw Materials	$0.57	$0.95
Utilities	$0.22	$0.15
Labor-Related	$0.06	$0.10
Capital-Related	$0.14	$0.23
Cost of Manufacture	$0.99	$1.42
SE, D, R&D, Adm, & I.C.	$0.27	$0.35
Cost of Sales	$1.26	$1.78
Pretax Earnings Based on 30% ROI	$0.52	$0.78
By-product Credits	$0.00	$0.00
Selling Price	$1.78	$2.55

5. Scope of the Study

In the current technoeconomic study of the ethanol process, the state of the art for its fermentative manufacture by the yeast: *Saccharomyces cerevisiae* was reviewed and compared with expected performance of the newer *Zymomonas* *mobilis* bacterium operating as immobilized cells in a fluidized bed bioreactor. From this, scenarios for an improved process were developed based on the expectations for adapting either system to reach plausible cell densities and effective concentration levels. The economics of these scenarios were then developed. The sensitivity of the economics to attaining, exceeding or falling short of goals for key operating parameters were also determined. It is hoped that the results will provide a strong perspective as to the relative merits for supporting research on any of the alternatives and the direction the research should be channeled so as to be economically relevant and improve the technoeconomic position of the process.

6. Bioprocess Problems

As noted earlier, fermentation processes have two major problems:

a) Inherently poor yields resulting from the production of by-products, including high levels of carbon dioxide needed to maintain the electronic balance of the metabolism of the organism, coupled with the current relatively high cost of renewable sugars and starches compared with the presently depressed prices for petroleum.

b) The inhibition of most organisms by their own products, which causes the fermentation to shut down after reaching only low product concentrations; as a result of which the recovery of product from dilute aqueous solution is accordingly expensive.

7. Yield and Raw Material Economics

Raw material economics has always been one of the most important parameters in determining the commercial viability of fermentation processes. In the United States, corn is the principal substrate for fermentation ethanol, comprising 77% of the grain used and 68% of all substrates. Substrate cost is determined by the combination of demand and price.

7.1 Substrate Demand

Product yield, as determined by fermentation stoichiometry, is obviously an important cost-determining factor [19-24]. Thus, the theoretical yield of ethanol from glucose amounts to 48 wt% for the yeast system and 50 wt% for the bacterium. In practice, the actual approach to theoretical is 90-95% for the yeast and about 98% for the bacterium because of the consumption of glucose for cell growth and maintenance. The difference arises because *Z. mobilis* consumes only one net ATP per glucose whereas *S. cerevisiae* gets two. Hence the cell yield per unit of glucose consumed for cells is twice as high for the bacterium as for the yeast [25,26].

Overall, then, even though the organisms are operating close to their biological limit, carbon yields for either system are poor as a result of large losses to carbon dioxide and sundry other by-products. Actual glucose demands amount to 2.19-2.31 pounds per pound of ethanol or 2.27-2.40 gallons of absolute alcohol per bushel of corn for the yeast and about 2.03 pounds per pound or 2.59 gallons per bushel for the bacterium, giving the latter a 7-12% competitive advantage in raw material costs.

7.2 Basis for Sugar Price

The cost of the sugar substrate is another very important element of cost; particularly if engineering improvements of the process can be realized.

As discussed in Section III, this study was based on the availability of a contract supply of a dilute 45% corn syrup from an adjoining wet mill at a transfer price of $0.065 per pound equivalent glucose [27]. In contrast, the cost of corn net of wet mill by-product credits has averaged $0.026 per pound equivalent glucose over the past 6 years [10]. Certainly the hydrolysis can be done better and cheaper as part of a large wet mill than as the mash operation used in older distilleries. In addition, handling hydrolysis as part of the wet mill rather than in fermentation eliminates tieing up expensive fermenters as slow hydrolysers.

7.3 Substrate Competitiveness

It cannot be expected that the yield of ethanol from sugar can be increased over its present biological limit. Consequently, further competitiveness of corn-based processes will have to depend on increases in the cost of crude oil relative to corn.

8. Product Inhibition

As with most fermentations, both *Saccharomyces cerevisiae* and *Zymomonas mobilis* are inhibited by their own substrate and products. Fermentation kinetics and process inhibition have been studied by a number of researchers for *Saccharomyces* [28-34] and *Zymomonas* [35-45]. Although agreement is not perfect, it appears that the yeast fermentation is totally inhibited by ethanol concentrations of about 105 g/l. The inhibitory cutoff for the bacterium is distinctly higher at 127 g/l. Furthermore, as shown in figure 27, the decay in specific productivity for *Zymomonas* is flat at 5.2 g product/g cells*liter up to a concentration of 55 g/l, after which inhibition begins. For the yeast the maximum specificity of 1.5 g/g*l drops over the whole range of concentration. Thus, as product concentration increases, specific productivity decreases, as does dilution rate for a fixed ratio of product to cells. This adverse effect has a profound influence on cost, and leads to a trade-off between maximizing concentration and maximizing dilution rate.

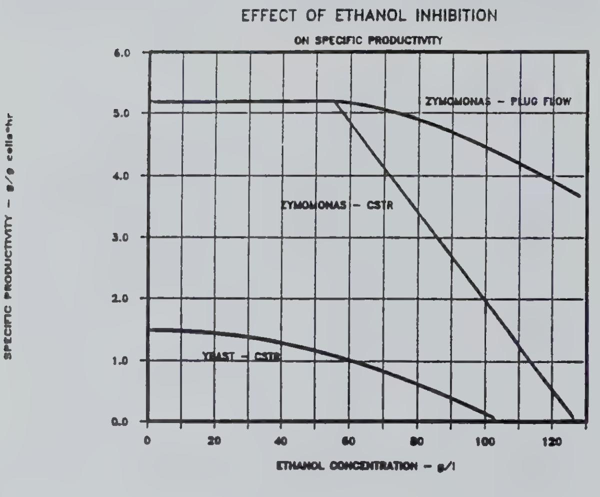


Figure 27

One possible solution to the inhibition problem would be to integrate the fermentation and distillation sections of the process so as to increase productivity while removing the product from the field of fermentation as rapidly as it forms. This is an automatic consequence of converting from a batch to a continuous process in which a proportionate increase in cell density is effected either by immobilizing the cells, as in the Oak Ridge case, to prevent their loss from the fermenter or by filtering the cells from the beer and recycling them while maintaining product concentration in the fermenter near the threshold of inhibition. The immobilization approach would be preferred since it would avoid passing cells through a filter and, possibly, a still with possible deactivation of cells by thermal or mechanical attrition with possible plugging of the trays of the still.

Thus, assuming that specific productivity (g product/g cell*hr) remains constant at constant (but maximum allowable) product concentration, the higher the cell density the greater the volumetric productivity (g product/l*hr), the shorter the fermentation time and, hence, the smaller the fermenter size and investment required for a desired design capacity; or for an existing fermentation plant, the greater the throughput and production level.

It appears then that the development of a continuous fermentation system is a fundamental requirement for improving the economic viability of the ethanol process. Continuous operation has been demonstrated at less than commercial scale by Bajpai and Margaritis [37], Ghose and Tyagi [29,46], Wilke [28,32,47], Davison and Scott [48,49] and others.

Scott and Davison [50] are operating a rack-scale 2.5-meter fluidized bed bioreactor at the Oak Ridge National Laboratory. The process is based on *Zymomonas mobilis* immobilized within 1.0-1.5 mm K-carrageenen beads at cell loadings of 15-50 g/l beads (6.6-22 g/l fermenter). The fermenter is operated in a continuous mode at 30 °C and pH 5.0. It was reported that plug-flow kinetics is achieved. Yield was reported to be 0.49 g ethanol/g glucose converted or 97.5% of the theoretical yield. Glucose spill is below 0.1% at an ethanol concentration of 74 g/l and a volumetric productivity of 60 g/l*hr. Volumetric productivity is normally in the range 50-120 g/l*hr but has reached 186 g/l*hr with 95% glucose conversion by recycling cells to higher density. This performance is in sharp contrast with the volumetric productivities of 1-2 g/l*hr usually reported by conventional yeast-based plants.

Alternatively, new organisms might be genetically engineered to be less inhibited by product and/or have a higher specific productivity than the wild strain.

9. Process Scenario for This Study

This study was based on using a fluidized bed bioreactor similar in design to the Oak Ridge approach. Cell density can be increased by either retaining cells in the fermenter or by recycling. For this study it was assumed that the beer leaving the fermenter train is passed to a filter unit to separate cells from the broth. The cell slurry is recycled except for a purge bleed equal to the amount produced.

A standard distillation train was assumed for the basecase. Greater heat economy might be realized by a more elaborate heat recovery scheme [15,16]. It would be interesting to compare the conventional design with cases based on using the Dartmouth IHOSR (Intermediate Heat Pumps and Optimal Sidestream Return) distillation process [51].

In either design the cell-free broth enters the first (beer) still of the distillation train, wherein the ethanol azeotrope and low boiling impurities are separated from salts, high boiling by-products and water. The aqueous tails from the stripping section are sent to waste disposal. No recovery of purged cells as distillers grains was assumed in this model. Fusel oils (amyl alcohols, mainly 3-methyl-1-butanol) are removed as a sidestream drawoff from the beer still. Low boilers are separated overhead in a refiner and the azeotrope is sent to a dehydration column to recover absolute ethanol.

10. Operating Scenario

It was assumed that the plant would be sited in the Midwest adjoining a corn wet mill. Capacity was sized to a 60-million gallons per year absolute ethanol plant with a midpoint of construction in 1986 and operating in 1990 at 90% utility. The investment estimates include a 30% contingency for undeveloped design, etc.

11. Economic Potential of Advanced Fermenter Systems

An economic model for the advanced fermenter system was used to explore the potential advantages of operating with cell recycle and/or improved specific productivity for both inhibited and non-inhibited systems of either *Saccharomyces cerevisiae* or *Zymomonas mobilis* under either batch or continuous modes.

The conversion economics of the ethanol fermentation process can be improved in two ways: (1) by increasing product concentration or (2) by increasing fermentation rate.

Of the two, increasing product concentration has the greater effect on cost. At any desired production level, the reciprocal of concentration—liters/gram—represents the volume of the equipment required for the complete process: media preparation, fermentation, product recovery, and product refining. Hence, concentration has a dominant effect on total process investment.

Fermentation rate affects only fermenter volume and investment. However, since fermenter investment usually accounts for a large part of total investment, the effect of rate on cost can be very large, indeed. At a fixed production level and product concentration, fermentation rate can be increased and fermenter volume decreased by increasing cell density, increasing specific productivity, or both.

Increasing cell density by containing the cells in an immobilized state in the fermenter or by recycling involves the appropriate engineering of the system under the constraints of broth viscosity and organism viability. However, increasing specific productivity involves producing a genetic change in the organism, which may be difficult to achieve in practice. Nevertheless, both approaches have merit and need to be pursued.

11.1 Inhibited Batch Systems Without Cell Recycle

Inhibited systems exhibit a minimum in cost as product concentration is increased up to the point of total inhibition. This effect is shown for the batch systems in Table 36 for a situation involving little or no cell recycle. (Cell density was held constant during the calculation of sensitivity, which means the cases at low concentrations had a small cell recycle involved.)

Table 36

ETHANOL EX S. CEREVISIAE
INHIBITED BATCH SYSTEM
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONC. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	FERMENTER INVEST'MT $million	FERM INV/ TOT PLANT INVEST'MT	CAPITAL COSTS $/gal	TOTAL COST $/gal
40	1.28	1.80	0.045	$52	38%	$1.13	$2.78
50	1.17	1.90	0.038	$48	40%	$1.03	$2.62
60	1.04	1.92	0.032	$48	42%	$0.97	$2.53
70	0.84	1.75	0.025	$52	46%	$0.96	$2.51
80	0.63	1.44	0.018	$63	53%	$1.02	$2.56
90	0.38	0.99	0.011	$94	64%	$1.24	$2.82
100	0.13	0.40	0.004	$255	83%	$2.53	$4.29

ETHANOL EX ZYMOMONAS MOBILIS
INHIBITED BATCH SYSTEM
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONC. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	FERMENTER INVEST'MT $million	FERM INV/ TOT PLANT INVEST'MT	CAPITAL COSTS $/gal	TOTAL COST $/gal
50	5.2	3.1	0.063	$29	29%	$0.87	$2.37
60	4.8	3.5	0.059	$26	28%	$0.79	$2.25
70	4.1	3.7	0.053	$25	29%	$0.74	$2.18
80	3.4	3.7	0.046	$25	31%	$0.71	$2.13
90	2.7	3.5	0.039	$26	33%	$0.70	$2.11
100	2.0	3.0	0.030	$30	37%	$0.71	$2.12
110	1.2	2.3	0.021	$41	46%	$0.78	$2.19
120	0.5	1.1	0.009	$84	64%	$1.11	$2.57

It should be noted that for the batch system, the term "dilution rate," as used in this study, refers to the reciprocal of the sum of batch time plus turnaround time, i.e., 1/(bt+tt). For the large fermenters used in the models a turnaround time of 12 hours was used for draining, cleaning, sterilizing, refilling and inoculating the fermenter after each batch run. This loss of time is not incurred in continuous operation, which, as will be seen, has a large effect on cost.

It should also be noted that specific productivity as used in this study refers to run time only, whereas volumetric productivity and dilution rate take into account the turnaround time for batch operation.

For the yeast, specific productivity and dilution rate are decreased ten-fold. However, because of the opposing effects of concentration versus productivity, volumetric productivity is maximized and fermenter investment is minimized at about 55 g/l. Capital charges and total cost are minimized at a higher concentration of about 70 g/l as a result of the effect of concentration on the rest of the plant as well.

The results for *Zymomonas* were similar except that the costs for the bacterium cases were always lower as a result of higher specific productivities, with a minimum cost of about $2.11 per gallon compared with a minimum of $2.51 for the yeast. In addition the bacterium can operate at concentrations higher than the yeast cutoff.

11.2 Inhibited Batch Systems With Cell Recycle

Cost is very sensitive to the recycle of cells. As shown in Table 37 cost decreases with increases in cell density at any product concentration. This effect mainly results from a concomitant reduction in fermenter investment. Total flow through a fermenter and specific productivity are fixed, irrespective of cell density, by fixing product concentration and annual production rate. Consequently as cell density is increased by recycle, fermentation time and volume (investment) can be correspondingly decreased in the design to balance production rate at a constant specific productivity.

For any product concentration, then, it is clearly desirable to operate at as high a cell recycle rate as possible. For example, Wilke operated at yeast concentrations up to 124 g dry wt/l at a volumetric productivity of 82 g/l*hr [28]; and Rogers reported operating with *Zymomonas* densities of 40 g/l for over 50 hours [40] at a volumetric productivity of 120 g/l*hr. However cell densities above these may produce unacceptable viscosities and adverse effects on the organism in the fermenter. This is an important point for further research clarification.

Table 37

ETHANOL EX S. CEREVISIAE
INHIBITED BATCH SYSTEM
EFFECT OF PRODUCT CONCENTRATION AND CELL RECYCLE
ON COST-PLUS-RETURN, $/GAL

PRODUCT CONC.-g/l	CELL DENSITY - g/l 5	10	20	50	100	150
40	$2.69	$2.62	$2.58	$2.54	$2.51	$2.49
50	$2.52	$2.45	$2.41	$2.37	$2.34	$2.33
60	$2.42	$2.33	$2.29	$2.26	$2.23	$2.22
70	$2.37	$2.27	$2.21	$2.17	$2.15	$2.14
80	$2.37	$2.24	$2.17	$2.12	$2.09	$2.08
90	$2.51	$2.28	$2.16	$2.09	$2.05	$2.04
100	$3.37	$2.69	$2.35	$2.14	$2.06	$2.03

ETHANOL EX ZYMOMONAS MOBILIS
INHIBITED BATCH SYSTEM
EFFECT OF PRODUCT CONCENTRATION AND CELL RECYCLE
ON COST-PLUS-RETURN, $/GAL

PRODUCT CONC.-g/l	CELL DENSITY - g/l 5	10	20	50	100	150
50	$2.33	$2.31	$2.30	$2.28	$2.26	$2.24
60	$2.21	$2.19	$2.18	$2.16	$2.15	$2.13
70	$2.13	$2.11	$2.10	$2.08	$2.06	$2.05
80	$2.07	$2.05	$2.03	$2.02	$2.00	$1.99
90	$2.04	$2.00	$1.99	$1.97	$1.95	$1.95
100	$2.02	$1.97	$1.95	$1.93	$1.92	$1.91
110	$2.04	$1.97	$1.93	$1.90	$1.89	$1.88
120	$2.21	$2.04	$1.95	$1.90	$1.87	$1.86

As a practical matter, it does not appear from the projections of Table 37 that increasing cell densities much above 50 g/l would have a significant effect on reducing further the cost of the product. At that cell density, the cost of ethanol by the yeast system at a concentration of 90 g/l would be $2.09 per gallon compared with $1.90 for the bacterium system at 110 g/l of product.

11.3 Inhibited Constant Environment Continuous Systems Without Cell Recycle

The very real advantage of operating in a continuous mode can be seen from the data of Table 38. It can be seen that volumetric productivity and dilution rate have values quite higher at low product concentrations than the respective cases for batch operation. The difference is related to batch turnaround time. At low concentrations, fermenter residence time is low and the relative adverse effect of turnaround is high; thus limiting dilution rates to low values. At high concentrations, fermenter time is very high and the effect of turnaround becomes insignificant, so that dilution rates for batch versus continuous operation approach each other.

Table 38

ETHANOL EX S. CEREVISIAE
INHIBITED CONTINUOUS SYSTEM
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONC. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	FERMENTER INVEST'MT $million	FERM INV/ TOT PLANT INVEST'MT	CAPITAL COSTS $/gal	TOTAL COST $/gal
40	1.28	3.88	0.097	$24	22%	$0.91	$2.52
50	1.17	3.54	0.071	$26	26%	$0.85	$2.41
60	1.06	3.15	0.052	$29	31%	$0.82	$2.36
70	0.84	2.53	0.036	$36	37%	$0.83	$2.36
80	0.63	1.89	0.024	$49	46%	$0.90	$2.42
90	0.38	1.14	0.013	$81	60%	$1.14	$2.69
100	0.13	0.38	0.004	$244	83%	$2.42	$4.15

ETHANOL EX ZYMOMONAS MOBILIS
INHIBITED CONTINUOUS SYSTEM - CONSTANT ENVIRONMENT
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONC. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	FERMENTER INVEST'MT $million	FERM INV/ TOT PLANT INVEST'MT	CAPITAL COSTS $/gal	TOTAL COST $/gal
50	5.2	12.7	0.254	$7	9%	$0.69	$2.17
60	4.8	11.8	0.197	$8	11%	$0.64	$2.08
70	4.1	10.1	0.144	$9	13%	$0.61	$2.03
80	3.4	8.3	0.106	$11	16%	$0.60	$2.00
90	2.7	6.5	0.072	$14	21%	$0.60	$2.00
100	2.0	4.8	0.048	$19	28%	$0.62	$2.01
110	1.2	3.0	0.027	$31	39%	$0.70	$2.10
120	0.5	1.2	0.010	$75	61%	$1.04	$2.48

Turnaround imposes a strict ceiling on effective dilution rate for batch operation. Thus even at a fermenter time of zero, dilution rate is held to $0.083\ \text{hr}^{-1}$ (1/12 hrs). Continuous operation is not so constrained and can approach effective dilution rates near infinity, at which the cost of fermenters become insignificant relative to total plant investment.

For operation without cell recycle in a constant environment, continuous mode, the yeast exhibits a minimum cost-plus-return price of $2.36 per gallon at a product concentration of about 65 g/l. The corresponding minimum price for the *Zymomonas* system is $2.00 at 85 g/l.

11.4 Inhibited Constant Environment Continuous Systems With Cell Recycle

The corresponding data for operation with cell recycle in a constant environment continuous system are shown in figure 28 for the yeast and figure 29 for the bacterium. For these cases, the minimum cost for the yeast at a cell density of 50 g/l is $1.97 per gallon at a product density of 90 g/l. For the bacterium the minimum for a cell density of 50 g/l is $1.81 at 110 g/l. As cell density is increased, the minimum in cost moves toward higher product concentrations.

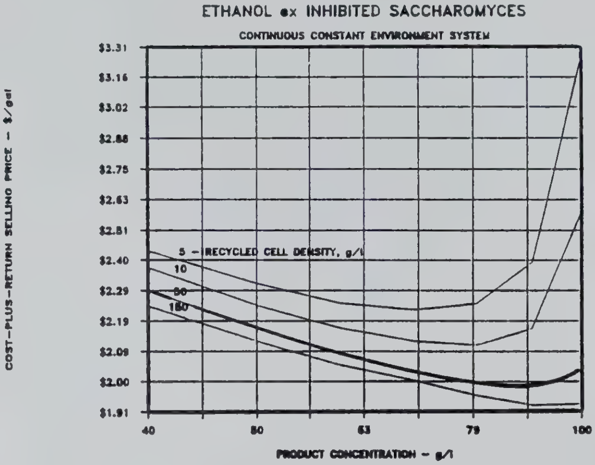


Figure 28

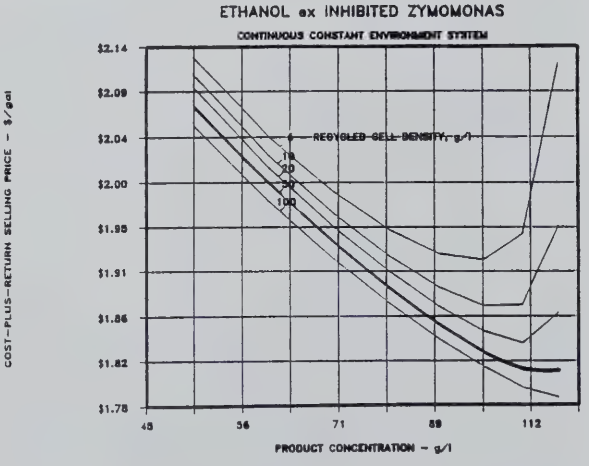


Figure 29

11.5 Inhibited Plug Flow Continuous Systems With Cell Recycle

It is well known that the kinetics of any first order reaction system are favored by operating in a plug flow regime. The effect on specific productivity of

Zymomonas was shown in figure 27. The cost data for plug flow operation with *Zymomonas* are shown in figure 30. In contrast to constant environment operation (Table 38), the decay in volumetric productivity and dilution rate with increases in product concentration is much less severe. Neither are minima exhibited within the field of the data shown. Minima have to exist with any inhibited system, but in this case occur at concentrations very close to total inhibition.

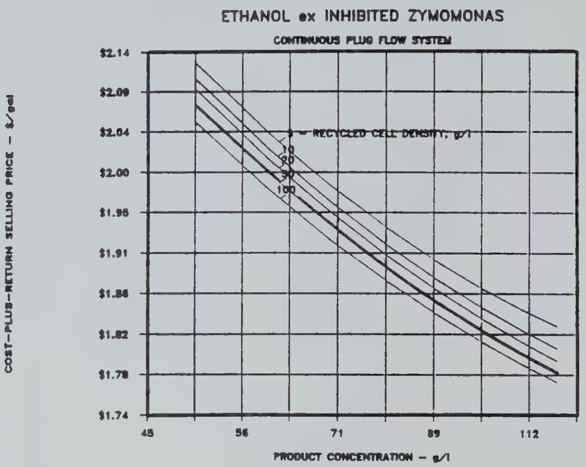


Figure 30

Without cell recycle, the case for using plug flow is very strong. Thus, plug flow at a cell density of 50 g/l and product concentration of 110 g/l exhibits a cost of $1.89 per gallon compared with a minimum cost of $2.00 for the constant environment case at the same cell density of 50 g/l but at an optimum product concentration of 85 g/l.

With the preferred cell recycle mode, the advantage of plug flow is lost. At high cell densities both regimes are approaching an effectively infinite dilution rate even at product concentrations up to 110 g/l which would otherwise favor plug flow. At high dilution rate the effect of fermenter investment is minimal. As a result both regimes exhibit costs of about $1.80 per gallon at a product concentration of 110 g/l.

11.6 Noninhibited Continuous Systems

It would be admittedly difficult to engineer an organism that is not inhibited by product. However if this could be accomplished with *Zymomonas* or *Saccharomyces cerevisiae*, cost would be reduced further according to the cost projections of figures 31 and 32. These depict a continuous system operating at various combinations of product concentration and dilution rates.

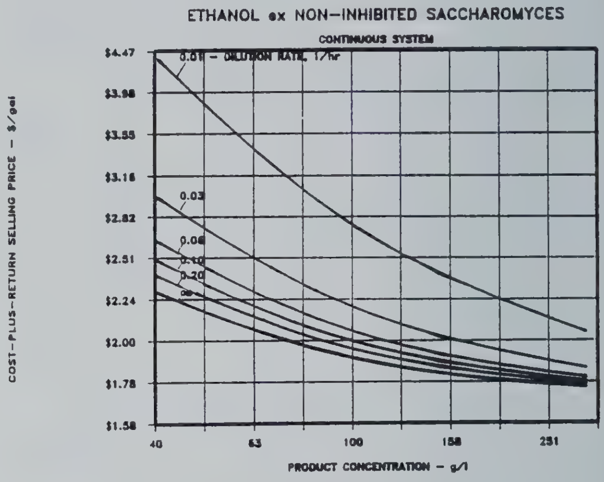


Figure 31

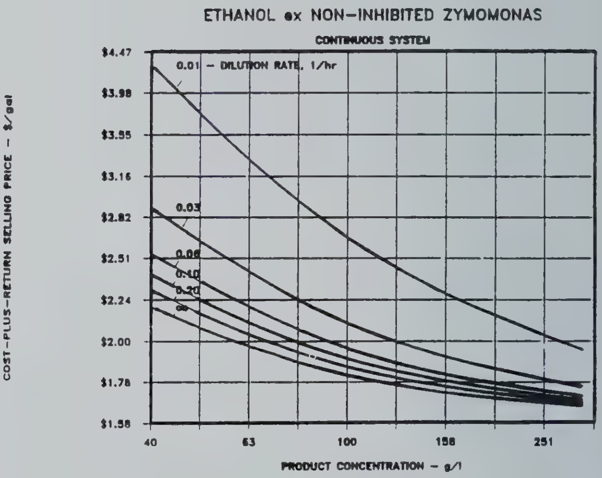


Figure 32

Dilution rate can be controlled independently of concentration by constraining or recycling cells to higher cell densities and/or by developing an organism with a higher specific productivity. For dilution rates below 0.083 hr^{-1} the data can also be used to represent batch operation. At high product concentrations dilution rates above 0.1 hr^{-1} converge near an infinite dilution rate.

For a dilution rate of 0.1 hr^{-1} at a product concentration of 150 g/l, the cost of ethanol from

Zymomonas would be reduced to $1.79 per gallon—a reduction of 30% below the $2.55 per gallon basecase cost for the current commercial state of the art. The corresponding cost for the yeast system would be $1.88—a 26% reduction.

11.7 Effect of Sugar Price

As noted earlier, the transfer price for glucose in the form of corn syrup is uncertain but quite important to the overall economics of the product. The sensitivity of cost-plus-return price to changes in the price of equivalent glucose is shown in figure 33 for an inhibited Zymomonas operating in a continuous constant environment system. At the assumed price of $0.065 per pound, ethanol price would be $2.00 per gallon; and substrate cost would account for 71% of the cost of manufacture and 44% of selling price. However at a bare "net corn" price of $0.038 per pound of sugar, the alcohol could sell for as little as $1.56 per gallon. Conversely, at a list price for syrup of $0.12 per pound the ethanol would have to sell for $2.56 per gallon. Clearly, the leverage of sugar price is very high.

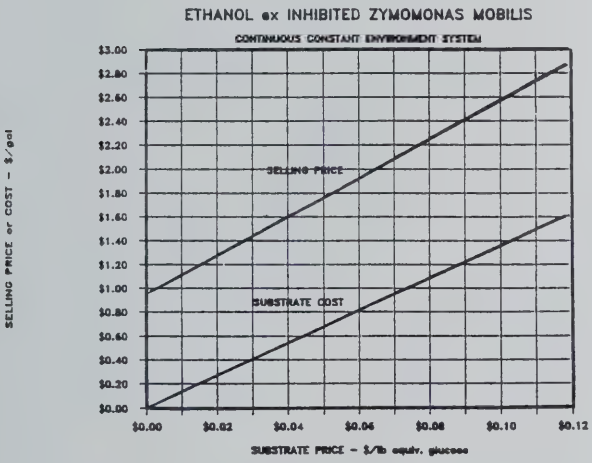


Figure 33

11.8 Glycerine Recovery?

With the exception of carbon dioxide, glycerine is formed at the highest concentration of any of the chemical by-products of the ethanol fermentation process; i.e., at 4.6 wt% for yeast and at 1.1 wt% for *Zymomonas*. A brief study was made of the economic feasibility of recovering glycerine in the distillation train of the yeast system. This requires the addition of a large still and reboiler to separate water and other lower boilers overhead from the glycerine in the tails. A smaller still is also required to remove glycerine overhead from residual salts and acids. It does not appear economical to recover glycerine in this way. Both expense and investment are adversely affected.

12. Strategies for Introducing the Advanced Technology

Obviously, much needs to be done in research at rack scale and pilot plant scale to prove out the projections described in this study. If that can be realized, however, a first step toward implementing the new systems might be to retrofit an existing fuel grade ethanol plant.

12.1 Retrofitting Existing Plants

It is beyond the scope of this study to evaluate the nuances of retrofitting existing plants. Too much depends on the design of the plant and the financial aspects of the supporting or ancillary businesses of the operator.

However as a first approximation, a case was developed based on introducing in 1990 an inhibited *Zymomonas* in a batch plant built around 1976. A sugar transfer price of $0.065 was assumed—the same as for the 1986 basecase but almost twice as high as the sugar price basis used in the 1976 plant of Table 35. The results are shown in Table 39. Product cost would be $1.69 by recycling to a cell density of 50 g/l at a product concentration of 110 g/l. This cost is in fact lower than the 1980 price of $1.79 even though the substrate cost is much higher.

For such a saving to be realistically obtained, the operator would have to exercise one of several options:

- Transferring the now excess fermenter investment off the ethanol books by: (1) writing down in place and taking the tax saving, or (2) applying the excess equipment to another venture;
- Expanding the investment base in medium preparation and product recovery and distillation to match the increased fermenter capacity at a higher production rate.

None of these options may be of interest to incumbent operators. It is suggested that studies be made pertinent to specific plant cases to develop a better picture of retrofitting possibilities.

Table 39

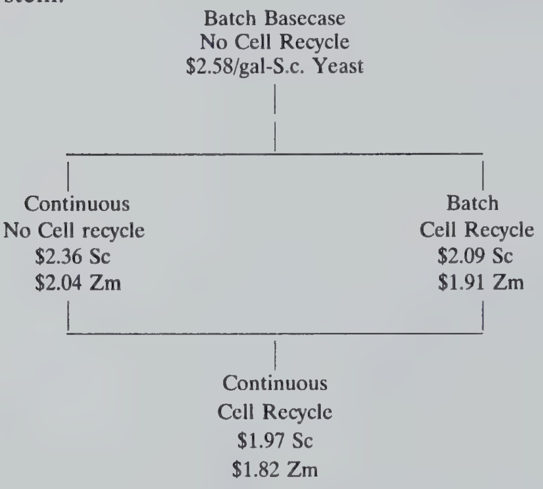
ETHANOL EX ZYMOMONAS MOBILIS
RETROFITTED PLANT* - INHIBITED BATCH SYSTEM
EFFECT OF PRODUCT CONCENTRATION AND CELL RECYCLE
ON COST-PLUS-RETURN, $/GAL

PRODUCT CONC.-g/1	CELL DENSITY - g/1 5	10	20	50	100
50	$1.96	$1.94	$1.93	$1.92	$1.90
60	$1.88	$1.87	$1.86	$1.85	$1.83
70	$1.83	$1.82	$1.81	$1.80	$1.78
80	$1.79	$1.78	$1.77	$1.76	$1.75
90	$1.76	$1.75	$1.74	$1.73	$1.72
100	$1.73	$1.72	$1.71	$1.70	$1.69
110	$1.71	$1.70	$1.69	$1.69	$1.68
120	$1.70	$1.69	$1.68	$1.67	$1.66
120	$1.70	$1.69	$1.68	$1.67	$1.66

* MPC-1976; Operating Year-1988; Substrate @ $0.065/1b

12.2 Design of New Plants

The most advantageous strategy for retrofitting or for the stepwise introduction of the new technology in new plants appears to follow the right-side path of the following alternatives for an inhibited system:



The financial performance of these cases is summarized in Tables 40 and 41.

13. Competitive Situation

With respect to the fuel ethanol (gasohol) market, competition is keen in a tight market situation. As of November 1992, thirteen companies had a combined standing capacity for about 1058 million annual gallons. This amount excludes the capacity of companies producing less than 10 million annual gallons. Archer-Daniel-Midland dominates the U.S. market with a capacity for 700 million gallons in four midwestern plants. Seven companies are in the process of installing an additional 160 million gallons; while 11 projects comprising a capacity for 530 million gallons are on hold as a result of the present uncertainty of an EPA ruling granting a waiver for the increase in volatility that ethanol

Table 40

OPTIMIZED PROCESS CONDITIONS
60 MM GPY ETHANOL MANUFACTURE
INHIBITED SACCHAROMYCES YEAST
1986 MPC - 1990 OPERATING YEAR

MODE	BATCH	BATCH	CONTINUOUS
Product Concentration - g/l	70	90	90
Cell Recycle	No	Yes	Yes
Cell Density - g/l	2.6	50	50
INVESTMENT-$Million			
Direct Permanent Investment	$94.0	$47.6	$35.3
Allocated Power, Services & Gen.	$26.8	$22.1	$22.1
Working Capital	$22.3	$19.2	$18.5
Total Investment	$143.1	$88.9	$75.9
COST-$/gal			
Raw Materials	$0.94	$0.95	$0.95
Utilities	$0.15	$0.13	$0.13
Labor-Related	$0.11	$0.10	$0.10
Capital-Related	$0.23	$0.13	$0.10
Cost of Manufacture	$1.43	$1.30	$1.27
SE, D, R&D, Adm, & I.C.	$0.36	$0.29	$0.28
Cost of Sales	$1.79	$1.59	$1.55
Pretax Earnings Based on 30% ROI	$0.79	$0.49	$0.42
By-product Credits	$0.00	$0.00	$0.00
Selling Price	$2.58	$2.09	$1.97

Table 41

OPTIMIZED PROCESS CONDITIONS
60 MM GPY ETHANOL MANUFACTURE
INHIBITED ZYMOMONAS BACTERIUM
1986 MPC - 1990 OPERATING YEAR

MODE	BATCH	CONTINUOUS	CONTINUOUS	BATCH	CONTINUOUS	CONTINUOUS
Product Concentration - g/1	90	90	90	110	110	110
Cell Recycle	No	No	No	Yes	Yes	Yes
Cell Density - g/1	1.8	1.8	1.8	50	50	50
Kinetics -Const Envirm't/Plug Flow	PF	CE	PF	PF	CE	PF
INVESTMENT-$Million						
Direct Permanent Investment	$61.7	$49.4	$41.3	$39.8	$29.7	$28.7
Allocated Power, Services & Gen.	$22.7	$22.7	$22.7	$19.6	$19.6	$19.6
Working Capital	$19.2	$18.5	$18.1	$17.6	$17.1	$17.0
Total Investment	$103.6	$90.7	$82.1	$77.0	$66.4	$65.3
COST-$/gal						
Raw Materials	$0.89	$0.89	$0.89	$0.89	$0.89	$0.89
Utilities	$0.12	$0.12	$0.12	$0.11	$0.11	$0.11
Labor-Related	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10
Capital-Related	$0.16	$0.13	$0.11	$0.11	$0.09	$0.08
Cost of Manufacture	$1.27	$1.25	$1.23	$1.21	$1.19	$1.18
SE, D, R&D, Adm, & I.C.	$0.30	$0.29	$0.28	$0.27	$0.26	$0.26
Cost of Sales	$1.58	$1.54	$1.51	$1.48	$1.45	$1.44
Pretax Earnings Based on 30% ROI	$0.58	$0.50	$0.46	$0.43	$0.37	$0.36
By-product Credits	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Selling Price	$2.15	$2.04	$1.96	$1.91	$1.82	$1.81

causes when added to gasoline. Increased volatility results in an increase in hydrocarbon emissions to the atmosphere [52].

Another concern is the competitive threat of methyl tert-butyl ether (MTBE), which is more compatible with gasoline and can be blended with gasoline at the refinery and shipped by pipeline. Ethanol must be blended at the terminal at the end of each pipeline to avoid water contamination and separation.

14. Conclusions

It appeared from the results of the study that improvements to either yeast or bacterium processes could be effective in reducing the cost of producing ethanol to commercially acceptable levels. However, the *Zymomonas* process would appear to be the better choice for development.

The use of continuous fermentation in a fluidized bioreactor system coupled with cell mobilization and/or recycle could substantially reduce the cost of ethanol and, generically, other products that are now produced at low concentrations and volumetric productivities as a result of product inhibition. Such an economic breakthrough cannot be realized until the system has been fully demonstrated in a continuous process over an extended period at pilot scale, optimized according to the findings of this study, and scaled up for the specific fermentation process of interest.

There appears to be no inherent design limitation in effecting the engineering improvements required in the process operation.

Such may not be the case in attempting to develop an organism with improved product tolerance and/or higher specific productivity. The goal is sufficiently important, however, to warrant the laboratory effort.

PART VI

Extractive Fermentation of Acetic Acid

Economic Trade-off Between Yield of Clostridium System and Concentration of Acetobacter System

Acetic acid is an example of a basic organic chemical that could be produced from renewable resources rather than fossil feedstocks. If corn were to become the sole source of acetic acid about 160 million bushels or 2% of the corn crop would be consumed for United States needs.

1. Scope of the Study

In this technoeconomic study of acetic acid process alternatives, the state of the art for its fermentative manufacture by the bacterium: *Acetobacter suboxydans* in the old vinegar process was reviewed and compared with expected performance of the newer *Clostridium thermoaceticum* bacterium. Both systems were projected to operate using immobilized cells in a fluidized bed bioreactor. From this, scenarios for an improved continuous process were developed based on the expectations for adapting either system to reach plausible cell densities and effective concentration levels.

The economics of these scenarios were then developed. The sensitivity of the economics to attaining, exceeding or falling short of goals for key operating parameters were also determined. It is hoped that the results will provide a strong perspective as to the relative merits for supporting research on any of the alternatives and the direction the research should be channeled so as to be economically relevant and improve the technoeconomic position of the process.

2. Historical Developments [1,2]

Acetic acid has been produced from ethanol as vinegar since ancient times by the "souring" of wine and beer. However, as with other organic chemicals, the introduction of cheap feedstocks based on petroleum and natural gas following World War II led to the demise of fermentation as a source of industrial acid. By 1981 acid production in the United States reached 2.7 billion pounds. Of this, one-third was produced by the liquid-phase oxidation of n-butane; one-third by the direct oxidation of ethylene (the Wacker process); and one-third by the now-preferred carbonylation of methanol (Monsanto or BASF processes) [3]. U.S. production in 1989 was 3.8 billion pounds, compared with a worldwide consumption of 8.0 billion pounds. Currently, about 62% of synthetic acetic acid is produced by the carbonylation process. All Wacker plants are shut down and fermentation is only used to produce vinegar for human consumption.

3. Fermentation Alternatives

Industrial acetic acid could be produced by either of two fermentation processes: (1) from corn hydrolysates in a two-step process by way of ethanol using *Acetobacter suboxydans* in an updated version of the old vinegar process; or (2) directly from corn syrup in a new process based on the thermophilic organism, *Clostridium thermoaceticum*. The stoichiometry of these fermentations is shown in figure 34.

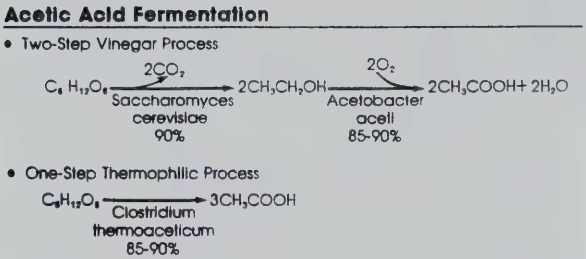

Acetic Acid Fermentation
• Two-Step Vinegar Process
$C_6H_{12}O_6 \xrightarrow{2CO_2} 2CH_3CH_2OH \xrightarrow{2O_2} 2CH_3COOH + 2H_2O$
Saccharomyces cerevisiae
90%
Acetobacter aceti
85-90%
• One-Step Thermophilic Process
$C_6H_{12}O_6 \longrightarrow 3CH_3COOH$
Clostridium thermoaceticum
85-90%

Figure 34

The *Acetobacter* process can operate at high (10 wt%) product concentrations and low pH but is limited to a maximum theoretical yield of two mols of acetic acid per mol of glucose consumed as a result of the corresponding yield of ethanol from glucose.

The *Clostridium* process produces acid at high rates accompanying elevated temperature operation and at yields near the theoretical three mols per mol of sugar. In spite of these rate and yield advantages, it is difficult to recover the product from the dilute beer. At the neutral pH required for satisfactory viability of the organism, the product occurs in dilute 20 g/l salt form. Acidification is required to recover the product by conventional recovery operations.

These process differences represent an economic trade-off between raw material costs and product recovery costs. The purpose of this study is to evaluate the trade-off from the point of view of determining the potential of either process for commercial development and guiding research in this area along economically relevant pathways.

3.1 Two-Step Acetobacter Process

In the vinegar process, ethanol is produced in the first step at 30 °C using conventionally the anaerobic yeast *Saccharomyces cerevisiae* at a yield of about 90%. In the second stage the aerobic bacterium *Acetobacter aceti* is used to convert the ethanol to acetic acid at a yield of about 85%.

In the early "quick" vinegar process the dilute alcohol, usually mixed with vinegar, was trickled down tall, wooden tanks packed with beechwood shavings or coke on which the bacteria lodged as "mother of vinegar" [4,5]. In later versions of the process, agitated baffled fermenters, similar to those used for penicillin, were used with cooling coils to control the exothermic reaction at 30 °C [6,7].

More recently, D.I.C. Wang using *Acetobacter suboxydans* was able to reach a maximum volumetric productivity in continuous culture of 11.5 g acetic acid/l*hr at a steady state acid concentration of 55 g/l, with cell recycle to a cell density of 7 g/l and at a dilution rate of 0.21 hr^{-1} [8]. This level was in contrast to typical productivities of commercial vinegar production of 0.5 g/l*hr [9]. At a pH of 2.8, substantially all the product was produced in free acid rather than salt form. Yield was 90-95%. Wang's study formed the basis for the two-step model evaluated in this study.

3.2 One-Step Thermophilic Process

In contrast to the vinegar process, *Clostridium thermoaceticum* converts glucose almost quantitatively to acetic acid [10]. Hence at an actual yield of 85-90% it has the potential for reducing significantly the raw material costs to two-thirds of those for the vinegar process. The organism is a thermophilic anaerobe which ferments glucose, xylose, or other sugars at 58 °C.

A basic problem, however, is that the organism prefers a neutral pH. As a result the product is in the form of an acetate salt rather than in the free acid form required to distill or extract the product from the fermenter broth. Schwartz and Keller of Union Carbide [11] approached this problem by attempting to adapt the organism to acid pH, thereby converting part of the salt in the broth to free acid. These results are compared in Table 36 with the data Wang obtained [12] while operating at neutral pH. As pH was reduced, productivity and product concentration dropped to unacceptable levels.

In a similar study Yates of Dupont [13] operated an 8-liter fermenter in a continuous mode without interruption for over 26,000 hours. Although conditions were varied over this period as part of the experimental program, acetate was produced at yields above 85% but at dilute concentrations of 0.25-0.30 M (15-18 g/l acid) similar to the results reported by Wang and Schwartz and Keller. Yates used a strain of *Clostridium thermoaceticum*

Table 42

Fermentation Performance

	Clostridium thermoaceticum					Acetobacter suboxidans
	Wang		Yates	Schwartz & Keller		Wang
Fermenter	Batch	Continuous	Continuous	Batch		Continuous
pH	6.8	6.8	6.0	5.5	4.5	2-8
Acetate – g/l (as acid)	45.	25.	18.	16.	4.	55-120
Productivity – g/l•hr	0.8*	8.0**	5.0	0.6	0.06	5.0
Yield – %	85-90	85-90	85-90	77.	85.	90-95
Minimum Glucose – g/gHAc	1.0	1.0	1.0	1.0	1.0	1.5
Temperature °C	60°	60°	58°	58°	58°	30°

*Free cells

**Immobilized Cells (2 if Free Cells)

obtained from L. G. Ljungdahl at the University of Georgia [14]. Both Yates and Schwartz and Keller used fermenter media that were too rich to be acceptable in commercial use. Clearly, further work is needed to adapt the organism to a cheaper acid medium without adverse trade-off in other important operating parameters. All three laboratories were making some progress in this regard when the projects were abandoned as a result of softening in oil prices.

4. Product Recovery Alternatives

The process selected for recovering the product as glacial acetic acid depends on whether the beer contains the product in free acid or salt form. Four alternatives are possible:

(1) The product occurs in acid form and is recovered as such;

(2) The product is produced in salt form but is acidified prior to recovery

(3) The product occurs as a salt and is simultaneously acidified and removed, e.g., electrodialysis; and

(4) The product occurs as a salt and is handled as such in the recovery operation. An example of the fourth alternative would be the proposed manufacture of calcium magnesium acetate for bridge and airport runway deicing. These approaches were considered in earlier studies [15-17]. Only the first two alternatives were considered in this study.

5. Recovery From Acid Form

In general, recovering fermentation products like acetic acid invariably involves separating the product from a dilute, usually under 10%, more generally 1-5%, aqueous solution.

Distillation can be used to recover products like ethanol which have boiling points below that of water, since in these cases the product is boiled away from large amounts of water [18,19]. However, energy costs for recovering high boiling products like acetic acid by distillation would be prohibitive. In such cases, large amounts of water would have to be distilled away from the product. Acetic acid and water are relatively close in volatility. To recover glacial acetic acid from a 1.5 wt% aqueous solution by simple distillation would require a column with a very high 2.8:1 reflux ratio at a steam load of 274,000 Btu/lb of acid recovered [20]. As a result, another approach—solvent extraction—was considered for this study.

5.1 Extraction With High-Boiling Solvent

In the case of extraction with a high-boiling solvent the product in the extract is distilled away from the solvent, thereby minimizing the thermal load on the system. It may prove difficult with this approach to prevent contaminating the aqueous raffinate with solvent if the raffinate is to be recycled (not in this study) or of contaminating the solvent with higher boiling materials if such are present.

There is a great deal of information in the literature dealing with the extraction of acetic acid from aqueous solution [21]. In the extraction process, the number of stages has a determining effect on extractor cost while the solvent to feed ratio, S/W, determines the cost of recovering the product from the solvent extract. Separation costs increase with increasing solvent ratios. It is important to use a solvent with as high a distribution coefficient, K_D, as possible since the product of K_D*(S/W) must be above 1.0 for adequate operation of a countercurrent extractor. At values approaching 1.0, the number of stages required for an acceptable separation approaches infinity. A value of K_D*(S/W) = 1.25 was used in this study as an optimum economic balance between number of stages and volumetric flow. King points out [22] that for extracting acetic acid at high dilution, distribution coefficients range from 1.68-0.64 for n-alcohols (C_4-C_8); 1.20-0.61 for ketones (C_4-C_{10}); 0.89-0.17 for acetates (C_4-C_{10}); and 0.63-0.14 for ethers (C_4-C_8). Although alcohols appear to be the best choice they esterify with acetic acid and are seldom used. Ketones are next in line but do not have good azeotroping properties for removal of water. Esters may exhibit chemical instability, particularly in acid pH [23], while hydrocarbons have poor coefficients. Esters and ethers are more commonly used, but none of these have outstanding distribution coefficients.

Yates [24] was able to show, however, in his study of the extraction of acetic acid from solutions simulating a fermentation beer, that the presence of salts in the aqueous phase greatly enhanced the distribution coefficient. He reported K_D's of 19 for tert-butanol, 14 for methylethylketone and 10 for sec-butanol in solutions containing 1.8 M sodium sulfate. The salt apparently has a salting out effect on solubilities and distribution coefficients. Othmer similarly noted improved K_D's of 4-6 for acetone, which becomes only partially miscible because of the high salt content [25].

King suggested that since acetic acid is a strong Lewis acid, a strong Lewis base should be ideal as a complexing solvent [26]. Tri-n-butyl phosphate gave coefficients of 2.3 at high dilution. The value varied linearly when mixed with hydrocarbon diluents. Trioctyl phosphine oxide (TOPO) at 50% in high-boiling ketones like 2-heptanone (150 °C) gave coefficients of 2.5 and solubility in water was only 1 ppm. Amines are also strong extractants for acetic acid and are less costly that TOPO. Tertiary amines should be used since primary amines are too water soluble and secondary amines are prone to irreversible amide formation. Alamine 336 (a commercial mixture of trioctyl/decyl amines) at 50% in diisobutylketone gave a coefficient of 2.5 and in 2-ethyl hexanol gave 6.0. Solubility in water was reported to be 10 ppm.

The choice of diluent is important in that it becomes an important solvating medium for the acid/amine complex leading to distribution coefficients higher than for either extractant or diluent alone.

5.2 Solvent Inhibition of the Organism

Although a lot of data exist on the extraction of acetic acid, little is available on the effects of such systems on the viability of the organism. For example, Wang [27] reported that sodium acetate had a strong inhibiting effect on the growth of *Clostridium thermoaceticum*, with complete inhibition of cell growth, although not acid production, at 48 g/l. Bar and Gainer [28] made a distinction between toxicity arising from solvent dissolved in the broth and that arising from presence of a separate solvent phase, as in in situ extraction within the fermenter. They found that cells of *L. delbrueckii* were not inhibited in a n-dodecanol-saturated broth but inhibited in a two phase system. Immobilizing the cells in carrageenan beads successfully protected the cells in the latter situation. These effects need further study.

6. Process Scenario Used for This Study

6.1 Process Description

From the preceding considerations it was decided to base the design of the technoeconomic model on the production of acid in fluidized bed bioreactors operating in a continuous mode with either *Clostridium thermoaceticum* on a glucose (corn syrup) substrate or *Acetobacter suboxydans* on ethanol. High cell densities would be developed in the fermenters by immobilization to prevent cell escape from the fermenter or by recycling after external filtration. Cells would be purged in the amount grown.

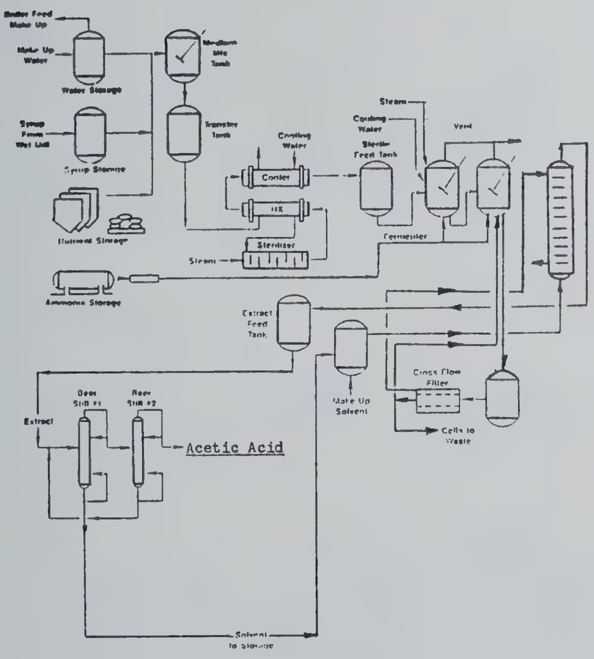
The ethanol would be similarly prepared in a fluidized bed bioreactor operated with the bacterium *Zymomonas mobilis* on a glucose substrate. The unconcentrated ethanol beer, after removing cells, would be sent to the *Acetobacter* fermenters. The acid broth after filtration would need no acidification and would be passed directly to the extractors.

For the *Clostridium* fermentation, pH would be controlled at 6.0 by ammonia that is also added as a nutrient. For a case where ammonium sulfate is recovered and sold as a fertilizer, the acetate filtrate leaving the filters would be evaporated to a 40% acetate concentration before feeding to the acidifier. Placing the evaporator in this position reduces the volume of aqueous medium handled in subsequent process steps.

Filtered and, in one case evaporated, *Clostridium* broth would be acidified with sulfuric acid to yield free acetic acid and ammonium sulfate as the feed to the extractors.

From any of these process options, the treated broth would be extracted in a continuous countercurrent multistage extractor using a high-boiling solvent like TOPO in a suitable carrier. It was assumed that the solvent would provide a distribution coefficient of 2.5 at a solvent/feed ratio of 0.5 and that a yield of acid to extract of 97% would be obtained through the use of an appropriate number of stages. It was also assumed that the solvent and water would have mutual solubilities less than 20 ppm, which would eliminate the need for a still to strip water off the acid product.

The extract would then be treated in a distillation column to separate solvent from acid product. Solvent would be recycled while product is sent to storage. A general flow chart for the process is shown in figure 35.



Process Model Used in Economic Study

Figure 35

(See page 133a
for enlarged view)

The salt solution appearing as the extractor raffinate would be sold as such without further purification or concentration, and with a minimum of storage.

If the salt has no commercial value and has to be purged as waste, no evaporation would be used. A soluble salt, like ammonium sulfate, would have to be disposed of by deep well flooding to prevent contamination of potable water aquifers. An insoluble salt, like calcium sulfate, could be disposed of in landfills.

6.2 Operating Conditions

The assumed basecase operating conditions for the plant are shown in Table 43. Four cases were evaluated:

(1A) *Acetobacter* at low pH
(1C) *Clostridium* with salt to waste
(2C) *Clostridium* with salt recovered and sold
(3C) *Clostridium* adapted to operate at low pH

Table 43

EXTRACTIVE FERMENTATION OF ACETIC ACID

BASECASE CONDITIONS

BACTERIUM	Acetobacter suboxydans	Clostridium thermoaceticum
SUBSTRATE	Ethanol	Glucose
Yield	92.5%	87.5%
Demand, g/g acetic acid	0.83*	1.14
FERMENTATION		
pH	2.8	6.0
Temperature C	30	58
Product Concentration, g/l	100	20
Cell Density - formed, g/l	4.2	1.4
- recycled**, g/l	50	50
Specific Productivity, g/g*hr	5.0	3.6
Dilution Rate, 1/hr	2.5	8.9
Volumetric Productivity, g/ℓ*hr	250	179
Fermentation Volume, gal	22,000	30,000

* Equivalent to a glucose demand of 1.68 g/g
** By immobilizing or recycling

EXTRACTION		
Solvent	50% TOPO in high boiling solvent	
Distribution Coefficient	2.5	2.5
Solvent/Aqueous Feed	0.5	0.5
Yield to Extract	97%	97%
Extractors		
Units	2	4***
Stages	10	10
Diameter, ft	8.8	11.6****

*** One for Case 2C with evaporated feed
**** 5.6 ft " " " " "

The data for the fermentations were based on the work of Wang and Yates, with reasonable extrapolations to higher cell densities. Similarly, the data for the extraction were based on the literature cited. It must be strongly stated, however, that none of the data represent more that small-scale research findings and that considerable research and development will be necessary to validate the conclusions of the study. Hopefully, the results will channel such research toward economically significant goals.

6.3 Site Scenario

It was assumed that the plant would be sited in the Midwest adjoining a corn wet mill with dilute, not evaporated, 45% syrup supplied over the fence by pipeline. Capacity was sized to a 250-million pound per year glacial acetic acid plant with a midpoint of construction in 1984 and operating in 1988 at 90% utility. The investment estimates include a 30% contingency for undeveloped design, etc. This uncertainty level is on the high side for designs based on reaming out existing facilities and on the low side for designs scaled up from semiworks data.

7. Economic Potential of Advanced Fermenter Systems

An economic model was developed to explore the potential advantages of operating an advanced fermenter system with cell recycle and/or improved specific productivity for both inhibited and non-inhibited systems.

The conversion economics of the acetic acid fermentation processes can be improved in two ways: (1) by increasing product concentration or (2) by increasing fermentation rate.

Of the two, increasing product concentration has the greater effect on cost. At any desired production level, the reciprocal of concentration—liters/gram—represents the volume of the equipment required for the complete process: media preparation, fermentation, product recovery, and product refining. Hence, concentration has a dominant effect on total process investment.

Fermentation rate affects only fermenter volume and investment. However, since fermenter investment usually accounts for a large part of total investment, the effect of rate on cost can be very large, indeed. At a fixed production level and product concentration, fermentation rate can be increased and fermenter volume decreased by increasing cell density, increasing specific productivity, or both.

Increasing cell density by containing the cells in an immobilized state in the fermenter or by recycling involves the appropriate engineering of the system under the constraints of broth viscosity and organism viability. However, increasing specific productivity involves producing a genetic change in the organism, which may be difficult to achieve in practice. Nevertheless, both approaches have merit and need to be pursued.

8. Overall Economic Comparisons

Of the cases studied only Case 3C, *Clostridium* adapted to low pH, appears competitive at current oil prices with synthetic acetic acid (Table 44). Its cost, including a 30% pretax return on investment, would be $0.32/lb compared with the 1Q90 synthetic acetic acid price of $0.29-$0.31/lb [29]. This case assumes that a *Clostridium* mutant organism can be adapted to operate without loss of efficiency at acid pH. This goal will probably be difficult to attain considering the only partial success of Yates and Schwartz and Keller in accomplishing it. However the leverage on reducing cost would be very great and worth the research effort.

Table 44

OPTIMIZED PROCESS CONDITIONS
250 MILLION PPY ACETIC ACID
CLOSTRIDIUM vs ACETOBACTER
1984 MPC - 1988 OPERATING YEAR

CASE MODE	1A	3C	2C	1C
Bacterium	A. s.	C. ta.	C. ta.	C. ta.
Scenario	Low pH No Salts	Low pH No Salts	Sulfate Recovered	Sulfate To Waste
Substrate	Ethanol	Glucose	Glucose	Glucose
Product Concentration - g/l	100	20	20	20
Cell Recycle - g/g formed	12:1	36:1	36:1	36:1
Cell Density - g/l	50	50	50	50
INVESTMENT-$Million				
Direct Permanent Investment	$39.2	$55.8	$77.5	$57.1
Allocated Power, Services & Gen.	$8.1	$17.8	$19.0	$17.8
Working Capital	$14.6	$11.0	$15.7	$41.3
Total Investment	$61.8	$84.6	$112.2	$116.2
COST-$/lb				
Raw Materials	$0.19	$0.08	$0.13	$0.13
Utilities	$0.01	$0.02	$0.05	$0.51
Labor-Related	$0.02	$0.02	$0.02	$0.02
Capital-Related	$0.02	$0.03	$0.05	$0.03
Cost of Manufacture	$0.24	$0.16	$0.25	$0.70
SE, D, R&D, Adm, & I.C.	$0.05	$0.05	$0.06	$0.12
Cost of Sales	$0.30	$0.21	$0.31	$0.82
Pretax Earnings Based on 30% ROI	$0.08	$0.11	$0.15	$0.15
By-product Credits	$0.00	$0.00	($0.04)	$0.00
Selling Price	$0.38	$0.32	$0.42	$0.98

This case, as with the remaining three, also assumes that cells can be built up to a density of 50 g/l without adverse effects. This goal appears quite reasonable in view of past successes with similar systems. For example Scott [30-32] operates currently with immobilized *Zymomonas* at 22 g/l and Rogers with free *Zymomonas* at 40 g/l [33-35]. Wilke operated the *Saccharomyces* yeast at cell densities up to 124 g/l with cell recycle [36].

Case 1A, *Acetobacter* operating at its customary acid pH, shows a slight edge over Case 2C, *Clostridium* at neutral pH with recovery of ammonium sulfate. At \$0.38 and \$0.42/lb respectively, neither could compete with the synthetic product at prices for petrochemical feedstocks. This comparison indicates that the better yield of *Clostridium*, which amounts to a saving in raw materials of \$0.06/lb, is not sufficient to make up for its low product concentration and higher plant investment (by \$50 million) even at the faster fermentation rate that accompanies operating at elevated temperatures.

Case 1C, in which dilute sulfate solutions are disposed of by deep welling, is completely out of the picture as a result of the extraordinary charges for waste disposal.

These cases will be reviewed in more detail in the following sections.

9. Acetobacter at Low pH

9.1 Raw Material Requirements

The greatest economic obstacle of the two-step process is high substrate demand. At the average overall yield, the process requires 2.0 g glucose/g ethanol and 0.83 g ethanol/g acetic acid for an overall sugar demand of 1.68 g glucose/g acetic acid.

The *Zymomonas mobilis* bacterial system was selected over the yeast *Saccharomyces cerevisiae* for producing ethanol because of the better yield of the former. Considering the simultaneous production of large amounts of carbon dioxide, hydrogen, and chemical by-products, the theoretical glucose demand for the overall reaction amounts to 531 mols glucose/1000 mols ethanol for the yeast system compared with 508 mols/1000 mols for the bacterial system.

Since these yields are near the theoretical maxima for the organisms involved, economic improvements to raw material costs will have to depend on cost advantages for corn compared with fossil feedstocks rather than on process improvements.

Because of the overall poor yield for this system, the effectiveness of the ethanol fermentation has a determining effect on overall cost for the acid. The cost of the sugar substrate at \$0.065/lb accounts for 62% of the transfer price for the dilute ethanol beer (Table 45), and the ethanol transfer price accounts for 50% of the \$0.38/lb cost-plus-return price for the acid (Table 46). If the sugar price increased to \$0.100/lb the price of acid would increase to \$0.46/lb, clearly out of contention with synthetic acid. Ultimately, then, the cost for acid will be controlled by the cost of corn relative to fossil materials. As noted earlier, the price history for these materials over the decade of the 1970's favors corn in the long run.

Table 45

ETHANOL FOR ACETIC ACID
30 MM GPY EX IMMOBILIZED ZYMOMONAS MOBILIS
FLUIDIZED BIOREACTOR - PLUG FLOW - CELL RECYCLE

BASIS	
Mid-point of Construction	1984
Operating Year	1988
Substrate - $/lb Equivalent Glucose	$0.065
INVESTMENT - $Million	
Direct Permanent Investment	$9.4
Allocated Power, Services & General	$0.8
Working Capital	$2.2
Total Investment	$12.3

COST - $/Unit	$/gal Ethanol	$/lb Acetic Acid
Raw Materials	$0.88	$0.117
Utilities	$0.01	$0.002
Labor-Related	$0.16	$0.021
Capital-Related	$0.04	$0.005
Cost of Manufacture	$1.09	$0.144
SE, D, R&D, Adm, & I.C.	$0.21	$0.028
Cost of Transfers	$1.30	$0.172
Pretax Earnings Based on 30% ROI	$0.12	$0.016
By-product Credits	$0.00	$0.000
Transfer Price	$1.42	$0.188

Table 46

ACETIC ACID MANUFACTURE
LOW pH ACETOBACTER FERMENTATION OF ETHANOL
EFFECT OF SUGAR PRICE ON ACID COST-PLUS-RETURN

SUGAR	ETHANOL COST					ACETIC ACID
$/lb	$/gal	$/lb	$/lb AA	% COM	% SP	$/lb
$0.000	$0.44	$0.067	$0.06	50%	26%	$0.22
$0.020	$0.74	$0.112	$0.10	63%	36%	$0.27
$0.038	$1.01	$0.153	$0.13	70%	42%	$0.31
$0.065	$1.43	$0.217	$0.19	77%	50%	$0.38
$0.080	$1.65	$0.251	$0.22	79%	52%	$0.41
$0.100	$1.96	$0.298	$0.26	82%	56%	$0.46
$0.120	$2.26	$0.343	$0.30	84%	58%	$0.51

9.2 Ethanol Fermentation

Because of the heavy burden of raw materials, the conversion process must be on the cutting edge of fermentation technology to compete. For this case process operating conditions appeared optimized at a product concentration of 100-110 g/l. As shown in Table 47 this point represents the optimum cost balance at a fixed 50 g/l cell density, although cost is relatively flat between 80-120 g/l.

Table 47

ETHANOL EX ZYMOMONAS MOBILIS
INHIBITED CONTINUOUS SYSTEM - CONSTANT ENVIRONMENT
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONCENT. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	TOTAL ETHANOL COST $/gal Ethanol	TOTAL ETHANOL COST $/lb Acetic Acd	CAPITAL COSTS $/gal	FERMENTER INVEST'MT $million
50	5.2	260	5.2	$1.53	$0.202	$0.25	$0.26
60	4.8	242	4.0	$1.50	$0.198	$0.23	$0.28
70	4.1	206	2.9	$1.48	$0.196	$0.21	$0.33
80	3.4	170	2.1	$1.46	$0.193	$0.20	$0.40
90	2.7	134	1.5	$1.45	$0.192	$0.19	$0.51
100	2.0	98	1.0	$1.44	$0.190	$0.18	$0.69
110	1.2	61	0.6	$1.44	$0.190	$0.18	$1.10
120	0.5	25	0.2	$1.46	$0.192	$0.19	$2.68

@ 50 g/l cell density

ETHANOL EX ZYMOMONAS MOBILIS
INHIBITED CONTINUOUS SYSTEM - PLUG FLOW
EFFECT OF PRODUCT CONCENTRATION

PRODUCT CONCENT. g/l	SPECIFIC PROD'ITY g/g*hr	VOLUME PROD'ITY g/l*hr	DILUTION RATE 1/hr	TOTAL ETHANOL COST $/gal Ethanol	TOTAL ETHANOL COST $/lb Acetic Acid	CAPITAL COSTS $/gal	FERMENTER INVEST'MT $million
50	5.2	260	5.2	$1.53	$0.202	$0.25	$0.26
60	5.2	259	4.3	$1.50	$0.198	$0.23	$0.26
70	5.1	254	3.6	$1.48	$0.195	$0.21	$0.27
80	4.9	246	3.1	$1.46	$0.193	$0.20	$0.28
90	4.7	235	2.6	$1.45	$0.191	$0.18	$0.29
100	4.5	223	2.2	$1.43	$0.189	$0.17	$0.30
110	4.2	210	1.9	$1.43	$0.188	$0.16	$0.32
120	3.9	196	1.6	$1.42	$0.187	$0.16	$0.34

@50 g/l cell density

Increasing product concentration decreases total plant investment. However, the attendant drop in specific productivity, resulting from increased product inhibition, decreases dilution rate and volumetric productivity and increases fermenter investment. Even close to the point of total inhibition at 127 g/l, volumetric productivity is high and fermenter investment relatively low. In this case it matters little whether the fermenter is operated with a constant environment ($1.44/gal) or with the usually preferred plug flow ($1.43/gal).

At a plant capacity of 250 million annual pounds of acid consuming 33 million gallons of ethanol, the economics are not particularly scale sensitive. The data indicate that a plant designed for 400 million pounds would only save $0.08 per gallon out of $1.43 in ethanol cost, which is equivalent to only $0.01/lb of acetic acid.

9.3 Acetobacter Fermentation

As with the other cases a recycle of cells to 50 g/l was assumed for this case. However cost is not very sensitive to this parameter. Restricting cell density to 4 g/l would only mean an increase in $0.014/lb in cost (Table 48). Again, the reason for this insensitivity is that the fermentation is already at very high volumetric productivities at which the influence of fermenter investment on total cost is very low.

Similarly, since *Acetobacter* already operates at a very high 100 g/l product concentration, increasing concentration further would not be a particularly rewarding research goal. For example at a 50 g/l cell density, an increase in product concentration to 200 g/l would only reduce price to $0.364/lb, corresponding to a $0.014/lb reduction in cost.

Table 48

ACETIC ACID MANUFACTURE
LOW pH ACETOBACTER FERMENTATION OF ETHANOL
EFFECT OF CELL RECYCLE ON COST

CELL DENSITY g/l	RECYCLE RATIO g/g formed	TOTAL COST $/lb	PLANT INVESTMENT TOTAL $MM	PLANT INVESTMENT FERMENTERS $MM	DILUTION RATE 1/hr	VOLUMETRIC PRODUC'ITY g/l*hr
4	0.0	$0.392	$52.6	$4.75	0.20	20
10	1.5	$0.384	$49.4	$2.13	0.50	50
25	5.4	$0.380	$47.9	$0.94	1.25	125
50	12.2	$0.378	$47.3	$0.51	2.50	250
75	19.5	$0.378	$47.1	$0.35	3.75	375

For 100 g/l product concentration; 5.0 g product/g cells*hr

9.4 Extraction

The effect of increasing solvent/feed ratio is indicated in Table 49. Total cost increases with increasing ratio over the entire range studied. Curiously enough, the investment in extractors was minimized at a ratio of 2.5. It appears that in order to maintain a constant yield of acid to extract of 97%, this ratio represents a balance between the effect of decreasing the number of stages required and increasing extractor diameter, as ratio and, hence, combined flow rate rises at a fixed feed flow. The effect is overwhelmed, however, by the increase in investment in distillation equipment to handle the solvent extract.

Table 49

ACETIC ACID MANUFACTURE
LOW pH ACETOBACTER FERMENTATION OF ETHANOL
EFFECT OF SOLVENT/BEER RATIO FOR K=2.5

SOLVENT/ BEER RATIO	TOTAL COST $/lb	INVESTMENT PLANT $MM	INVESTMENT EXTRACTORS $MM	INVESTMENT STILLS $MM
0.5	$0.378	$47.3	$2.24	$1.97
1.0	$0.382	$48.2	$1.46	$2.23
1.5	$0.388	$49.9	$1.43	$2.50
2.0	$0.394	$51.8	$1.55	$2.78
2.5	$0.400	$53.6	$1.49	$3.07
3.0	$0.407	$55.5	$1.60	$3.37
4.0	$0.420	$59.8	$2.10	$3.99
6.0	$0.446	$68.0	$2.83	$5.31

For 97% yield acetic acid to extract

Provided the solvent does not inhibit the organism, it is very important to identify a solvent for acetic acid with as high a distribution coefficient and selectivity as possible. Even so, as indicated in Table 50, increasing the coefficient beyond the basecase assumption of 2.5 does not appear particularly rewarding.

10. Clostridium at Neutral pH With Salt Recovery

Salts in neutral *Clostridium* broths would have to be acidified to recover free acetic acid. It was assumed that ammonia would be used for both fermenter pH control and cell growth; and that ammonium acetate in the broth would be acidified with sulfuric acid to form free acetic acid and ammonium sulfate. Ammonium sulfate is highly soluble in water (706 g/1000 g). For Case 2C it was assumed that it would be recovered as a 40% solution for sale as a fertilizer. The ammonium sulfate solution is evaporated and sold.

There is considerable precedent for doing this. Since 1960 a major source of ammonium sulfate has been as a by-product in manufacturing caprolactam for nylon 6. About four pounds of salt are produced for each pound of caprolactam. The salt is usually used as a 40% solution [25]. Low nitrogen content makes shipping long distances uneconomical. However a plant located in the Midwest would be surrounded by agricultural customers. Ammonium sulfate is an exceptionally good fertilizer for rice and might be barged down river to the rice areas of Arkansas, Louisiana and Texas. However, even with the sale of by-product salt, the very high cost penalty of having to operate the *Clostridium* fermentation at neutral pH can be readily seen by comparing the economics for Cases 3C and 2C on Table 44. Selling price is increased \$0.10/lb, or 30% over the extrapolated case at low pH. A \$0.040/lb acetic acid credit for ammonium sulfate does not even cover the \$0.052/lb increase in raw materials cost created by the need for additional ammonia and sulfuric acid. In addition higher steam and electrical demands for evaporation and other processing increase utility costs by \$0.033/lb. Similarly, a large increase in plant investment of \$22.9 million or 31% increases capital charges by \$0.052/lb. Plant investment is detailed in Table 51. The most expensive section becomes the addition of evaporators (falling film type with vapor recompression) [37-39] and acidification equipment.

Sulfate selling price does not have a major effect on acid cost. This is shown in Table 52. A basecase price for ammonium sulfate of \$70/ton was selected to be on the low side of the published range of \$60-\$120/ton [29]. If the salt were given away, cost would rise about \$0.045/lb acid or 11%. The analysis assumes that storage of the salt solution during off seasons for fertilization would be at the expense of dealers rather than the manufacturer.

Eliminating product inhibition would have a greater effect on reducing cost for this case than for Case 3C. Most of the additional cost for the sulfate basecase relates to handling and evaporating large quantities of water from a dilute 20 g/l solution. It allowable product concentration were increased to 100 g/l, the cost for acetic acid would be cut nearly in half to \$0.25/lb; i.e., substantially under the price for synthetic acid and only \$0.01/lb higher than the price of the product from the low

Table 50

ACETIC ACID MANUFACTURE
LOW pH ACETOBACTER FERMENTATION OF ETHANOL
EFFECT OF DISTRIBUTION COEFFICIENT

DISTRIBUTION COEFFICIENT K	TOTAL COST \$/lb	INVESTMENT			EXTRACTORS			
		PLANT \$MM	STILLS \$MM	EXTRACTORS \$MM	CAPACITY FACTOR	DIAMETER ft	STAGES	UNITS
0.5	\$0.404	\$55.2	\$3.07	\$2.98	5411	10.8	10	2
1.0	\$0.387	\$50.1	\$2.37	\$2.38	4884	9.2	10	2
1.5	\$0.382	\$48.4	\$2.14	\$2.24	4420	8.8	10	2
2.0	\$0.379	\$47.7	\$2.03	\$2.21	4009	8.8	10	2
2.5	\$0.378	\$47.3	\$1.97	\$2.24	3645	8.8	10	2
3.0	\$0.377	\$47.1	\$1.92	\$2.31	3320	9.0	10	2
4.0	\$0.377	\$46.9	\$1.87	\$2.49	2769	9.5	10	2
6.0	\$0.377	\$47.2	\$1.81	\$3.01	1958	10.9	10	2

For 97% yield acetic acid to extract; S/W = 1.25/K

Table 51

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION WITH SALT RECOVERY
PLANT INVESTMENT

	$Million	% Plant
Total Plant Investment	$96.5	100%
Evaporation & Acidification	$28.3	29%
Receiving, Prep & Sterilization	$23.6	24%
Product/Cell Separation	$13.4	14%
Product Storage	$9.2	10%
Allocated Electrical	$6.3	7%
Allocated Steam	$3.8	4%
Distillation	$1.7	1.8%
Fermentation	$0.7	0.7%
Extraction	$0.6	0.7%
Other Plant Investment	$8.9	9%

Table 52

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION WITH SALT RECOVERY
EFFECT OF SULFATE CREDIT ON ACID COST

SULFATE PRICE $/TON	SULFATE CREDIT $/lb AA	ACID COST $/lb
$0	$0.000	$0.469
$40	($0.023)	$0.443
$70	($0.040)	$0.424
$100	($0.057)	$0.404
$130	($0.074)	$0.385

For 20 g product/l; 50 g cells/l

pH *Clostridium* case at 100 g/l (Table 53). *Accordingly, eliminating product inhibition so as to increase concentration would be a very rewarding research goal even for an organism that requires a neutral environment.*

The data show that it would be less rewarding to work on increasing cell density, optimizing solvent/beer ratio, or increasing distribution coefficient as long as plant investment is dominated by equipment related to salt recovery.

Although sugar to acid yield is good for this case, sugar price does have a large effect, as is shown in Table 54.

Table 53

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION WITH SALT RECOVERY
SENSITIVITY OF ACID COST, $/lb

PRODUCT CONC, g/l	CELL DENSITY, g/l 10	50
20	$0.44	$0.42
40	$0.32	$0.32
60	$0.29	$0.28
100	$0.25	$0.25
150	$0.24	$0.23

For 3.57 g product/g cells*hr

Table 54

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION WITH SALT RECOVERY
EFFECT OF SUGAR PRICE ON ACID COST-PLUS-RETURN

SUGAR PRICE	--------SUGAR COST--------			ACETIC ACID
$/lb	$/lb AA	% COM	% SP	$/lb
$0.000	$0.00	0%	0%	$0.33
$0.040	$0.05	21%	12%	$0.39
$0.065	$0.08	30%	18%	$0.42
$0.080	$0.10	35%	21%	$0.45
$0.100	$0.12	40%	25%	$0.47
$0.120	$0.14	45%	29%	$0.50

11. Clostridium at Neutral pH With Salt to Waste

Case 1C outlines the situation in which a sulfate salt from the acidification operation must be disposed of as a waste stream. The case shown is for ammonium sulfate, a soluble salt, and as a result represents a "worse case" scenario. It is very difficult to dispose of soluble salts. For this case it was assumed that the ammonium sulfate solution would be pumped down a deep well into brackish strata below aquifers of potable water. According to studies made by the Environmental Protection Agency this type of disposal costs about $20 per ton of *total* solution [40]. For a dilute 20 g/l sulfate solution this cost amounts to $0.49/lb acetic acid and results in a total acid cost of $0.96/lb.

Obviously this disposal method cannot be used for dilute solutions. In the unlikely event, however, that product concentration in fermentation could be substantially increased, the cost of disposing of a soluble salt would be reduced accordingly. This effect is shown in Table 55.

Table 55

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION - SALT TO WASTE
EFFECT OF DEEP WELL DISPOSAL COST ON ACID COST

DISPOSAL COST $/ton*	----20 g product/l---- TOTAL $/lb AA	DISPOSAL COST $/lb AA	%Total	----150 g product/l---- TOTAL $/lb AA	DISPOSAL COST $/lb AA	%Total
$0	$0.39	$0.00	0%	$0.28	$0.00	0%
$5	$0.53	$0.12	23%	$0.30	$0.02	5%
$10	$0.67	$0.24	36%	$0.32	$0.03	10%
$20	$0.96	$0.49	51%	$0.35	$0.06	18%
$30	$1.25	$0.73	58%	$0.39	$0.10	24%

* Based on total volume of 2.3% ammcnium sulfate solution
Cells recycled to 50 g/l

If the disposal method were free the cost of acid would drop to $0.39/lb, which is lower than the $0.42/lb selling price calculated for Case 2C in which the ammonium sulfate solution is evaporated and sold.

A cheaper alternative to deep welling would be land filling of an insoluble salt. The cost of land filling is independent of the concentration of product and amounts to about $80/dry ton. Consequently a salt for deep welling would have to be at a concentration above 25 wt% before it could compete. A land fill alternative could be based on using lime to control pH in the *Clostridium* fermentation. Calcium acetate has a solubility of 327 g/1000 g water at 60 °C. This concentration is equivalent to an acetic acid concentration of 124 g/l, which is considerably above presently attainable concentrations and, hence, the salt would remain soluble during fermentation. During acidification, waste gypsum (calcium sulfate) would be formed at a rate of over a pound for every pound of acetic acid produced. It has a solubility at 50 °C of only 2.6 g/1000 g water and would precipitate and be removed by adding a filtration step to Case 1C. The cost of landfilling would be only $0.047/lb acetic acid, or a saving of $0.442/lb acid over deep well disposal costs. This saving would drop the cost of acetic acid to $0.54/lb—still a very high cost compared with other options.

12. Clostridium Adapted to Low pH

In Case 3C it was assumed that a mutant could be genetically engineered to operate at low pH. Even with this adaptation, at a usual product concentration of 20/g/l, it will be very important to operate at high cell densities to overcome the adverse effect of low concentration. This effect is shown in Table 56. Operating without recycle or confinement of cells would increase cost to $0.36/lb or $0.045/lb or 14% above the basecase at 50 g/l. However cell densities above 50 g/l do not appear to provide more than a few mils in savings. At 50 g/l and above, volumetric productivity is so high that further decreases in fermenter investment have little effect on cost.

In addition to the important goal of adapting to acid conditions, it would be very rewarding to develop an organism that is not inhibited by product. For example at a cell density of 50 g/l, a *Clostridium* that could operate at 100 g product/l, as does *Acetobacter,* would provide a reduction in cost to $0.22/lb (Table 57). This selling price would be 30% below the basecase and $0.07-$0.09/lb below the current price of $0.29-$0.31/lb for synthetic acid.

Table 56

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION AT LOW pH
EFFECT OF CELL RECYCLE ON ACID COST-PLUS-RETURN

CELL DENSITY g/l	RECYCLE RATIO g/g formed	TOTAL COST $/lb	PLANT INVESTMENT TOTAL $MM	FERMENTER $MM	DILUTION RATE 1/hr	VOLUMETRIC PRODUC'ITY g/l*hr
1.4	0	$0.361	$94	$18.6	0.3	5
5	3	$0.329	$79	$5.3	0.9	18
10	6	$0.323	$76	$2.9	1.8	36
25	17	$0.318	$74	$1.3	4.5	89
50	36	$0.316	$73	$0.7	8.9	179
75	57	$0.315	$73	$0.5	13.4	268
100	80	$0.314	$73	$0.4	17.9	357

For 20 g product/l; 3.57 g product/g cells*hr

Table 57

ACETIC ACID MANUFACTURE
CLOSTRIDIUM FERMENTATION AT LOW pH
SENSITIVITY OF COST-PLUS-RETURN PRICE, $/lb

PRODUCT CONC, g/l	CELL DENSITY, g/l 10.00	50.00
20	$0.32	$0.31
40	$0.27	$0.26
60	$0.24	$0.24
100	$0.23	$0.22
150	$0.22	$0.22

For 3.57 g product/g cells*hr

13. Process Development Strategy

13.1 Product Inhibition

Although *Acetobacter* and *Zymomonas* can tolerate product concentrations up to at least 100 g/l, *Clostridium thermoaceticum* is highly inhibited and limited to acetate concentrations of about 20 g/l. Hopefully, an organism might be genetically engineered that is not inhibited by product and can tolerate low pH. However, this goal may be very difficult to attain.

13.2 Cell Immobilization/Recycle

Short of this, the best fermentation strategy appears to be to control product concentration at the optimum level vis-a-vis product inhibition while operating at as high a cell density as is physically and/or biologically possible. Assuming a constant specific productivity at an optimum product concentration, this operating strategy fixes dilution rate at a maximum level and minimizes fermenter size and investment. An attempt was made in this study to define the optima within the limitations of published data.

13.3 Continuous Mode

It also appears that the development of a continuous fermentation system is a fundamental requirement for improving the economic viability of the acetic acid process. As noted previously, Yates operated a small laboratory fermenter for thousands of hours with *Clostridium thermoaceticum* without problems.

Scott and Davison [41] are operating a rack-scale 2.5-meter fluidized bed bioreactor in a continuous mode at the Oak Ridge National Laboratory on various organisms including *Clostridia* and *Zymomonas mobilis*. The process is based on cells immobilized within 1.0-1.5 mm K-carrageenan beads at cell loadings of 15-50 g/l beads (6.6-22 g/l fermenter). For *Zymomonas* it was reported that plug-flow kinetics are achieved. Yield was reported to be 0.49 g ethanol/g glucose converted or 97.5% of the theoretical yield. Glucose spill is below 0.1% at an ethanol concentration of 74 g/l and a volumetric productivity of 60 g/l*hr. Volumetric productivity is normally in the range 50-120 g/l*hr but has reached 186 g/l*hr with 95% glucose conversion by recycling cells to higher density. This performance is in sharp contrast with the volumetric productivities of 1-2 g/l*hr usually reported by conventional fermentation systems.

14. Strategies for Introducing the Advanced Technology

Obviously, much needs to be done in research at rack scale and pilot plant scale to prove out the projections described in this study. If that can be realized, however, a first step toward implementing the new systems might be to retrofit part or all of an existing fuel grade ethanol plant to the *Acetobacter* fermentation.

However, it is beyond the scope of this study to evaluate the nuances of retrofitting such plants. Too much depends on the design of the plant and the financial aspects of the supporting or ancillary businesses of the operator. If any of the options are of interest to existing operators, it is suggested that studies be made pertinent to specific plant cases to develop a better picture of retrofitting possibilities.

15. Conclusions

Based on the economic analyses it appears that the use of continuous fermentation in a fluidized bioreactor system coupled with cell immobilization and/or recycle could substantially reduce the cost of acetic acid and, generically, other organic acids that are now produced at low product concentrations and volumetric productivities as a result of product inhibition. Such an economic breakthrough cannot be realized until the system has been fully demonstrated in a continuous process over an extended period at pilot scale, optimized according to the findings of this study, and scaled up for the specific fermentation process of interest.

However there appears to be no inherent design limitation in effecting the engineering improvements required in the process operation.

Such may not be the case in attempting to develop an organism with improved product tolerance and/or higher specific productivity. The goal is sufficiently important, however, to warrant the laboratory effort.

PART VII

Extractive Fermentation of Solvents

Technoeconomic Comparison Between Single-Stage In Situ Extraction and Multistage External Extraction

1. Introduction

As with other fermentations, the production of the solvents: acetone, butanol, and ethanol by the bacterium *Clostridium acetobutylicum* exhibits poor yields on glucose and severe product inhibition limits concentrations to commercially unacceptable levels, e.g., 10-15 g/l butanol.

In this technoeconomic study of the "ABE" process, the state of the art for its fermentative manufacture is defined. From this, scenarios for an improved process are developed based on the expectations for adapting extractive fermentation to reach plausible cell densities and effective concentration levels. The economics of these scenarios are then developed. The sensitivity of the economics to attaining, exceeding or falling short of goals for key operating parameters were also determined. It is hoped that the results will provide a strong perspective as to the relative merits for supporting research on any of the alternatives and the direction the research should be channeled so as to be economically relevant and improve the technoeconomic position of the process.

2. Market Position

The United States leads among world producers of butanol [1]. Production has risen steadily at 5% annually since 1964 to a production level of about 918 million pounds of n-butanol plus 190 million pounds of isobutanol. European production is less and stagnant; Japanese production has declined to where Japan is now a net importer.

Almost all butanol is made from propylene by the Oxo process. Consumption favors n-butanol in all market areas, but especially in U.S. markets. As a result newer plants are based on a rhodium catalyst system that enhances the production of n-butanol, the preferred isomer.

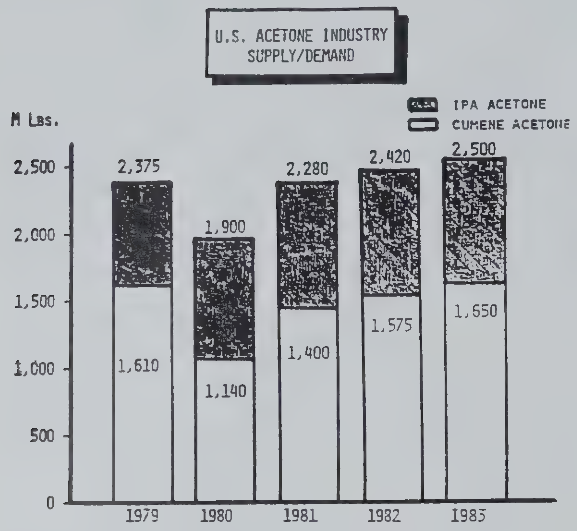
Million Pounds	n-Butanol	Isobutanol	n/iso
United States	842	143	5.9
Europe	300	220	1.4
Japan	43	36	2.6

The major U.S. end uses for n-butanol in descending order are: for butyl acrylates/methacrylates for latex paints, textile finishes, and floor polishes; glycol ethers as solvents for surface coatings and adhesives; butyl acetate as a rapid drying solvent for varnishes; dibutylphthalate and other plasticizers for a variety of adhesives, packaging films, and surface coatings; amino acids; butylamines for use in pesticides and rubber processing; and uses in fire-resistant hydraulic fluids. Demand reached 920 million pounds in 1988 and is expected to increase by 3.2-3.5% annually.

Isobutanol has similar uses but favors direct solvent use. It also finds use in lube oil additives. It is generally inferior to n-butanol in properties and finds use only if price is sufficiently discounted—historically 15%.

Use of n-butanol and isobutanol in blends with methanol as an octane enhancer for gasoline has been introduced but has faced environmental challenges and stiff competition from Oxinol tert-butanol blends and ethanol blends. Economics do not appear attractive compared with methanol/ethanol blends. However butanol might find better use as blends with diesel oil and with jet fuel for military aircraft.

Acetone, the primary by-product in butanol manufacture by fermentation, has actually a more important role than butanol in world markets. Demand in the United States over the decade of the 1980's has been relatively flat at about 2.5 billion pounds. Most of this has been for producing methacrylates or acrylic resins (fig. 36). It must be noted that the acetone supply is derived from two sources: [1] as a by-product in the conversion of cumene to phenol, or [2] by direct synthesis from isopropanol. U.S. producers are listed in Table 58 according to their raw material basis. By-product acetone tracks the demand for adhesives for plywood for the building trades and is always sold off first at a discount under the cost of isopropylene-derived product. Accordingly, acetone derived from fermentation must either compete with the latter or be discounted as the former. Recent producers of sugar-derived acetone are listed in Table 59. Of these only the plant in South Africa is significant.



	1979	1980	1981	1982	1983
CUMENE ACETONE IN-PLACE CAP.	2,053	2,137	2,368	2,368	2,368
IPA ACETONE IN-PLACE CAP.	990	1,040	1,190	1,190	1,190
TOTAL IN-PLACE CAPACITY	3,043	3,177	3,558	3,558	3,558

Figure 36

Table 58

U.S. ACETONE PRODUCERS
"IN-PLACE" CAPACITIES

M̄ POUNDS

PRODUCER	1980	1981	1982	1983	1984
CUMENE BASED					
ALLIED	360	360	360	360	360
CHEVRON	33	33	33	33	33
CLARK	54	54	54	54	54
DOW	284	284	284	284	284
GENERAL ELECTRIC	30	240	240	240	240
GEORGIA PACIFIC	177	198	198	198	198
GETTY (SKELLY)	57	57	57	57	57
MONSANTO	300	300	300	300	300
SHELL	300	300	300	300	300
U.C.C.	230	230	230	230	230
U.S. STEEL	312	312	312	312	312
SUB TOTAL	2,137	2,368	2,368	2,368	2,368
[redacted]					
EASTMAN	80	80	80	80	80
EXXON	140	140	140	140	140
SHELL	650	800	800	800	800
U.C.C.	170	170	170	170	170
SUB TOTAL	1,040	1,190	1,190	1,190	1,190
GRAND TOTAL	3,177	3,558	3,558	3,558	3,558

3. Historical Development

The original Weizmann process for fermenting starch-containing grains to butanol and acetone was developed under the stimulus of the World War I demand for acetone for manufacturing "cordite," a double-based smokeless powder used for British naval guns. The process made a successful transition to civilian products but was finally supplanted in the 1950's by cheaper petrochemical processes. Interest in the fermentation process revived following the energy crisis of 1973 but was cooled again as a result of the softening in oil prices in the early 1980's [2].

A few years prior to World War I, Dr. Chiam Weizmann had developed an organism, *Clostridium acetobutylicum*, which successfully fermented starchy grains to produce a mixture of acetone, butanol and ethanol. He applied for and received patents on the so-called ABE process [3,4].

With the outbreak of World War I a plant was built at Kings Lynn, England in 1914 to produce acetone by fermentation, but operation was a

Table 59

ACETONE EX BIOSUGAR

Producers	Status
National Chemical Products Co. Transvaal, Union So. Africa	Operating 12 X 25 M gal.
Egyptian Sugar & Distillation Co. El-Hawamdia, Giza, A.R.E.	Operating
Soviet Union	Operating
Commercial Solvents Corp. Terre Haute, IN	Torn Down 50 M gal.
Chase Chemical Puerto Rico	Torn Down 2 X 60 M gal.
Publicker Industries Philadelphia, PA	Standby 140 MM PPY 5 X 2000 M gal. (EtOH) 10 X 500 " 9 X 250 " 12 X 18 " 6 X 1 "

failure until Weizmann was placed in charge and installed his process. Because of the shortage of corn in England, the process was transferred to Canada in August 1916, where it operated until November 1918. To supplement this output a butanol-acetone plant was built in Terre Haute, Indiana which operated from May to November 1918 under the auspices of the War Production Board. While the Terre Haute Plant operated there was no use for butanol and it was stored.

However shortly after the end of the war the Dupont Company developed Duco nitrocellulose lacquers for use in automobile finishes. It was found that n-butyl acetate was the solvent of choice for this coating system. In order to supply the n-butanol required for making the acetate, the Terre Haute plant was reactivated in 1920 as a private venture by Commercial Solvents Corporation, which had acquired an exclusive license under the Weizmann U.S. patent. Commercial Solvents used 50,000 gallon fermenters to make the solvents. The plant is now owned by International Minerals and Chemical Corporation. It no longer operates the fermentation equipment but has maintained the historical cultures and has advised that the technology is available for licensing.

When the patents expired in 1936 new ABE plants were built in Philadelphia (Publicker), Baltimore, Puerto Rico, and Japan. A flow sheet for the process as practiced by Publicker in the late 1930's and 1940's is shown in figure 37. The Publicker plant was based on the use of 5000-gallon Hortonspheres through 500,000 gallon tanks for the batch fermenter train. Operation of this plant was described in detail by Beesch [5]. The plant was, since, shut down, but was considered for reactivation in the late 1970's. The decision to proceed was deferred as a result of the oil glut of the 1980's.

At the present time the only ABE plant operating in the free world is at Germiston in the Union of South Africa at National Chemical Products, Ltd., a division of Sentrachem Ltd. The plant was started up in 1936. Its operation was described by Spivey [6].

4. Technical Background

4.1 Raw Material Demand

Raw material economics has always been one of the most important parameters in the choice between fermentation processes for producing solvents. Until 1938 the ABE process operated solely on corn using *Clostridium acetobutylicum* with a solvents yield of about 26.5% based on dry corn and comprising roughly 60% butanol, 30% acetone and 10% ethanol [7-9]. After 1938 new organisms were developed which allowed the use of cheaper molasses.

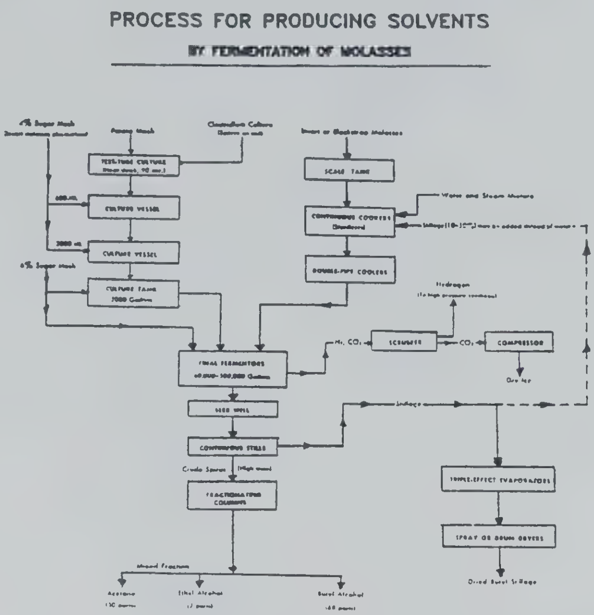
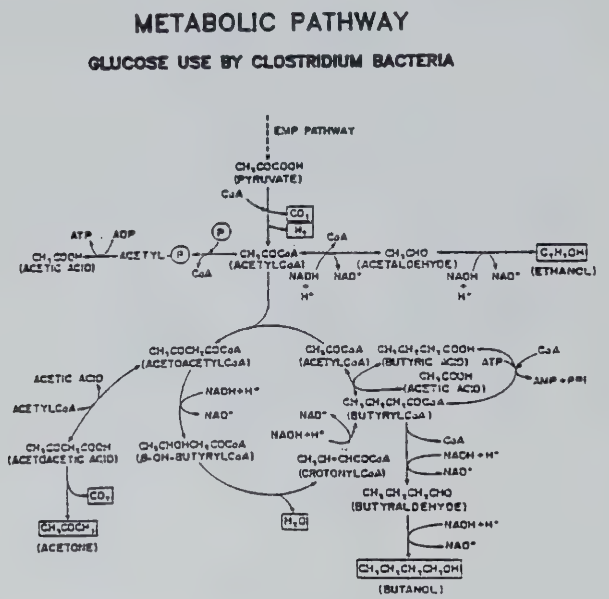


Figure 37
(See page 133b
for enlarged view)

Early in this study it became apparent that the stoichiometry of the fermentation was very important to the economics. The metabolic pathway followed by *Clostridium acetobutylicum* is outlined in figure 38. Electron balance must be maintained among the competing reactions. Yields to the various products are outlined in Table 60. Even though the organism operates near its biological maximum, carbon yields are poor because of the large losses to carbon dioxide. In general, the solvents are formed in the ratio: 60% n-butanol, 30% acetone, and 10% ethanol with the corresponding release of hydrogen and carbon dioxide.

Alternatively, Weimer has postulated that an organism could be developed that would produce only butanol according to the "goal" case of Table 60. This could theoretically be accomplished, although with great difficulty, by blocking the acetyl CoA to acetaldehyde (to ethanol) pathway and the acetoacetyl CoA to acetone pathway [10]. Small amounts of acetaldehyde might be added to the fermentation to inhibit the ethanol route, but since acetaldehyde is toxic in general, it might completely stop the fermentation.



(See page 133c
for enlarged view)

Figure 38

Table 60

Fermentation Stoichiometry
(per 100 Moles of Butanol)

Base Case

Glucose $\longrightarrow$ Butanol + $2CO_2$ + H_2O
100.0 100.0 200.0 100.0

Glucose $\longrightarrow$ Acetone + $3CO_2$ + $4H_2$
40.0 40.0 120.0 159.8

Glucose + $2H_2O$ $\longrightarrow$ 2Acetic Acid + $2CO_2$ + $4H_2O$
12.5 12.5 25.0 25.0 50.0

Glucose $\longrightarrow$ 2Ethanol + $2CO_2$
8.3 16.6 16.6

Glucose $\longrightarrow$ Butyric Acid + $2CO_2$ + $2H_2O$
6.7 6.7 13.5 13.5

167.5 Glucose $\longrightarrow$ 100.0 Butanol + 40.0 Acetone
+ 25.0 Acetic Acid + 16.6 Ethanol
+ 6.7 Butyric Acid + 375.0 CO_2
+ 35.0 H_2O + 223.4 H_2

Goal Case

100.0 Glucose $\longrightarrow$ 100 Butanol + 200.0 CO_2 + 100 H_2O

4.2 Product Inhibition

As with most fermentations, *Clostridium acetobutylicum* is inhibited by its own substrate and products. Previous studies have shown that butanol is the most toxic of the products [11,12]. The fermentation is totally inhibited by butanol concentrations of 10-15 g/l [2,13,14]. Thus, in normal batch operation, productivity is limited to about 0.25 g/(l)(hr), i.e., 13 g/l butanol after forty batch hours plus twelve hours of fermenter turnaround. Productivities in the range 0.16-0.58 g/(l)(hr) have been reported by various investigators. [10-15] *This experience has suggested to many that the fermentation rate and product concentration could be raised to commercial levels by removing the butanol from the fermentation medium as fast as it forms*. This assumption forms the basis for the scenarios developed for economic evaluation in this study.

Various methods for removing inhibitory products have been proposed. These include: adsorption by activated carbon [15-18], ion exchange resins [19-22], or polymeric resins [23-26]; extraction by aqueous solvents [27-33] or organic solvents [34-40]; or membrane separation [41,42]. The use of organic solvents is the subject of the butanol study.

As a preamble to extraction studies, a number of laboratories have tested the toxicity of various solvents toward the organism [35,37,38] [43-48]. In many cases it was found that good solvents for the products were also toxic to the organism.

In the early 1980's Leung of MIT [43] studied at small scale the extraction of butanol with corn oil during fermentation to minimize inhibition.

Gill and Ratledge [49] suggested that the toxicity of hydrocarbons toward specific organisms might be related to the aqueous solubility of these compounds. They showed that toxicity was reduced by adding a nontoxic compound such as hexadecane to the organic phase.

Evans and Wang at Michigan [50] studied extractive fermentation at a 10 ml test tube scale with the aim of optimizing distribution coefficient versus toxicity by using mixtures of toxic solvents having good distribution coefficients with nontoxic hydrocarbons having low solubility in the aqueous fermentation medium. Oleyl alcohol was found to be a good solvent with low toxicity.

Japanese investigators also demonstrated the use of oleyl alcohol to extract butanol in batch experiments [37].

Blanch and coworkers at the University of California at Berkeley [51] also showed in limited small scale tests using oleyl alcohol as a solvent that the effect of butanol inhibition could be reduced and volumetric productivity increased by removing butanol in either batch [52] or fed-batch culture [53]. The feasibility of using continuous processing in extractive fermentation was also demonstrated at bench scale in experiments in which the fermenter broth was continuously recycled to an external extraction column [54]. In the fed-batch experiments using oleyl alcohol as a solvent they were able to increase productivity to 1.5 g/(l)(hr). However, in these experiments productivity can also be inhibited by the high concentrations of the sugar substrate required in batch culture to drive the fermentation to high butanol productivities. True continuous culture would circumvent this problem. Blanch's continuous runs were operated for over 55 hours at double the productivity of batch or fed-batch culture.

In normal batch operation, productivity is limited to about 0.25 g/(l)(hr), i.e., 13 g/l butanol after 40 batch hours plus 12 hours of fermenter turnaround. Productivities in the range 0.16-0.58 g/(l)(hr) have been reported by various investigators [31,37,39,40,54,55].

The extractive fermentation program at Battelle Memorial Institute picked up where these studies left off. Since early 1986 Battelle has been developing its "multi-phase fluidized bed (MPFB) bioreactor" concept with the intent to enhance fermentation by removing product as fast as it forms using an in situ solvent (oleyl alcohol, etc.) that is not soluble in the aqueous fermentation medium and non toxic to the organism. A schematic drawing of the Battelle bioreactor concept is shown in figure 38. This design was used to represent the fermenters in this study. The production of butanol/acetone/ethanol by *Clostridium acetobutylicum* was chosen as the demonstration example for the generic process. The program has since been transferred to the Oak Ridge National Laboratory. If successful with this system, the Oak Ridge program will be expanded to the acetic acid, ethanol, and other systems.

The goals of the program are to: (1) demonstrate the feasibility of the MPFB bioreactor for producing bulk chemicals in a continuous mode and (2) provide a generic design basis which can be scaled up beyond the current pre-pilot scale to the commercial production of butanol as well as other major products.

The program to date has been aimed at developing a cell immobilization system; testing this in a fluidized bed reactor; determining in separate tests the toxicity of the candidate solvents for butanol toward the immobilized organism; and in the course of all this to design, build and operate a process development unit (pre-pilot plant) to study operation. Progress has been reported in a number of papers [56-60].

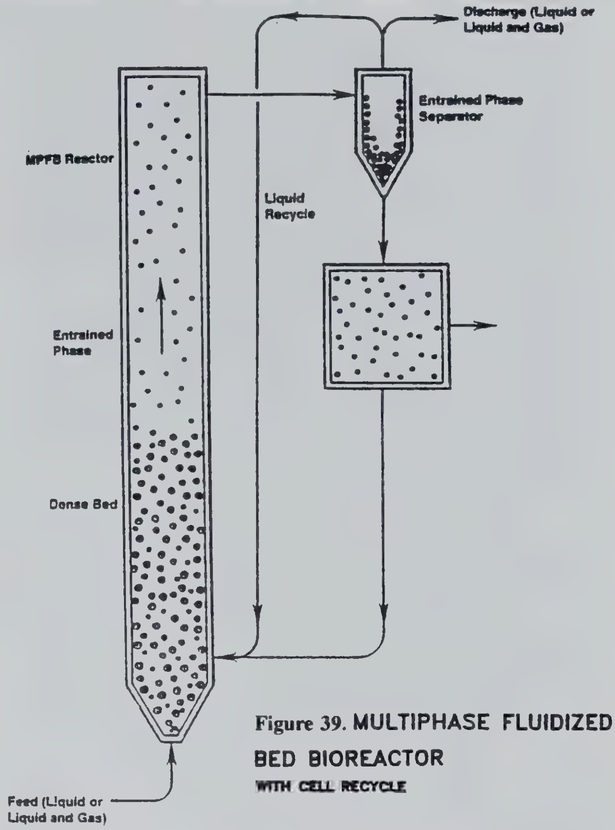

Discharge (Liquid or Liquid and Gas)
Entrained Phase Separator
MPFB Reactor
Liquid Recycle
Entrained Phase
Dense Bed
Feed (Liquid or Liquid and Gas)

Figure 39. MULTIPHASE FLUIDIZED BED BIOREACTOR WITH CELL RECYCLE

5. Process Development Strategy

5.1 Batch Mode

In the operation of the conventional batch fermenter on *Clostridium acetobutylicum*, it is well known that as the product accumulates in the fermenter a point is reached at which product inhibition of the functioning of the organism shuts down the fermentation. The amount of product produced is controlled by the volume of the fermenter at the maximum attainable product concentration—usually a low amount.

In view of this limitation of the batch system, many researchers have evaluated the advantages of removing product from the batch fermenter "as fast as it forms" by various means in order to sustain the fermentation over a longer period. In such cases additional substrate must be added in such a manner as to not adversely affect the fermentation by substrate inhibition. This condition usually results in the use of a fed-batch mode.

In effect, however, this approach actually represents a conversion of the batch mode to a continuous mode in which cells are prevented from leaving the fermenter. Thus, in any continuous system the product is always being removed from the fermenter as fast as it forms.

5.2 Continuous Mode

It appears then that the development of a continuous fermentation system is a fundamental requirement for improving the economic viability of the butanol process. As noted earlier, Blanch has operated a small research unit in a continuous mode, as has Scott of Oak Ridge National Laboratory [61]. Scott incorporates lactic acid in an immobilized cell system to act as a mild hydrogen donor to scavenge oxygen so as to maintain a strict anaerobic environment and prevent cell deactivation. These results are encouraging, but it is imperative that continuous operation be demonstrated over an extended period at pilot scale.

This study was based on a continuous fermentation system in which product is removed from the broth either by an external, multistage extractor or by the in situ, single stage extraction of product within the fermenter itself. The two approaches differ in that in the external case the beer (at the maximum allowable, but low, product concentration) is the *feed* to a multistage extraction; whereas in the in situ case the same beer is the *raffinate* leaving a single stage extraction. In the latter case the *"effective concentration"* in the fermenter (the "feed" to the in situ extraction) can be 10-15 times higher than in the aqueous beer phase, although the single stage extraction is not as efficient as the multistage approach. Work is underway now to develop a model based on an in situ multistage extractor/fermenter design.

5.2.1 External Multistage Extractor This study was based on a continuous fermentation system in which cells are maintained in the fermenter at a desired, maximum level. Thus, assuming that specific productivity (g product/g cell*hr) remains constant at constant (but maximum allowable) product concentration, the higher the cell density the greater the volumetric productivity (g product/l*hr), the shorter the fermentation time and, hence, the smaller the fermenter size and investment required for a desired design capacity; or for an existing fermentation plant, the greater the throughput and production level.

This result can be accomplished either by immobilizing the cells to prevent their loss from the fermenter or by filtering the cells from the beer and recycling them. The immobilization approach would be preferred since it would avoid passing cells through a filter and, possibly, an extractor with possible deactivation of cells by mechanical attrition or exposure to solvent and with possible plugging of the trays of an extractor.

If for some reason the cells cannot be immobilized, then, two alternative recycle schemes can be considered: (1) a single recycle in which the cells are carried with the beer through an extractor and recycled with raffinate to the fermenter, or (2) a double recycle in which the cells are separated from the beer before the extractor and recycled while cell-free raffinate from the extractor is recycled separately so as to assist in recovering by-products.

The economic consequences for any of the above options would be the same except for certain limiting situations.

5.2.2 External Extraction with Single Recycle The single recycle mode was used as the basis for this study as a "worse" case. It has the drawback that recycled cell density and recycled raffinate cannot be controlled separately. Thus for this model a point is reached at a recycle ratio of 15:1 beyond which recycle supplies all the need for make up water in the fresh feed. To go higher would require that the 45% syrup feed to the fermenter be evaporated to maintain the water balance. This would greatly increase the cost of substrate and must be avoided.

This limitation may be moot, however, since at a 15:1 recycle, cell density has been increased from 1.4 g/l at zero recycle to 22.3 g/l, dilution rate from 0.03 hr^{-1} to 0.48 hr^{-1} and volumetric productivity from 0.4 to 6.3 g/l*hr. As a result, total plant investment has been reduced from $228 million to $41 million for a 160 million pound per year production level and the cost-plus-return selling price from $1.08/lb butanol to $0.43/lb. Although cell density could presumably be increased above 22 g/l without adverse effect, further increases would lead to marginal improvements in cost.

5.2.3 External Extraction With Double Recycle In the double recycle case, cell density could reach higher levels than are possible with the water balance limitations of the single recycle case. Likewise cells would have less exposure to solvent with concomitant possible toxic side effects. Process control would have to be more sophisticated, but this is not an insurmountable problem.

In either recycle case the recycle of raffinate is mainly desirable to reduce product losses to the aqueous purge. It also reduces the fluid load on the first raffinate still thereby reducing the cost of this large still and its attendant steam consumption and investment. Raffinate recycle is also ostensibly desirable to: (1) enhance the extraction of less extractable by-products such as acetone and ethanol;

(2) conserve process water; and (3) to recycle cells in the single recycle case. None of the latter arguments are critical to the process. For the basis of this study, the recovery of low-boiling chemicals by distillation of the raffinate is definitely economically justified. This prevents the loss at any recycle ratio of valuable by-products that are not recovered by extraction. Conservation of process water is of minor importance compared with other cost elements. As noted, cell recycle can be accomplished by separate recycle or immobilization.

5.2.4 In Situ Extraction In the in situ case cells are either recycled, immobilized or allowed to grow in a first stage fermenter to the level required to produce the desired amount of product in a second stage, such that the raffinate (beer) leaving the fermenter does not exceed the threshold level of inhibition of product concentration. The effective concentration, i.e., amount produced divided by the aqueous flow, would be many times this since the bulk of the product leaves in the solvent extract. The multiplier would approximately equal the solvent/feed ratio times the distribution coefficient (about 12× for the basis used).

In summary then, in external extraction, cell density is increased to reduce fermentation time and fermenter volume at the maximum allowable product concentration in the beer for a desired production level. In in situ extraction cell density is increased to increase effective product concentration at the maximum allowable product concentration in the aqueous beer and constant fermentation time for the desired production level.

6. Extractive Fermentation Process Scenarios

6.1 Process Scenario for External Extraction

A flowsheet for the process model of external extraction is shown in Figure 40. Beer leaving the fermenter train is passed to a multistage extractor (or first to a filter in the double recycle model) whereupon substantially all of the product is removed by a selective solvent. Some of the by-product acetone and ethanol are removed also, as are the higher boiling acids: acetic and butyric. Actually as a worse case it was assumed, rather than known, that the acids would be, indeed, produced and that the pH of extraction would be low enough for the acids to exist as acids rather than as salts. In salt form they could not be extracted and would stay with the raffinate.

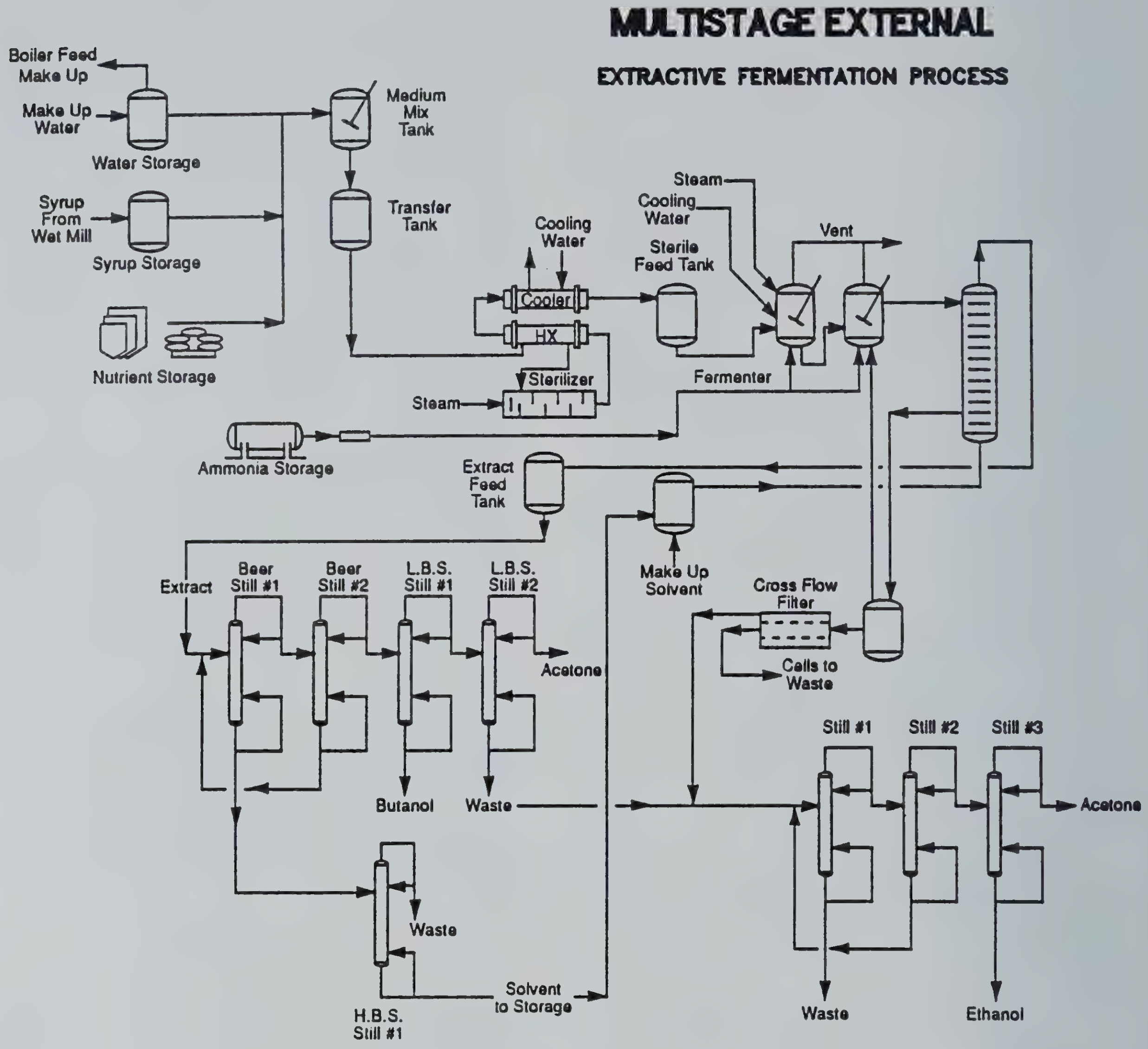
The aqueous raffinate, containing cells in the single recycle case, leaving the extractor is recycled to the desired, highest possible level to the fermenter. The balance is filtered to remove residual cells. The filtrate is sent to the raffinate still train to recover by-product acetone and ethanol. Residual salts either fed to or produced in the fermenters are purged as the tails from the first raffinate still.

Butanol, by-product acetone and ethanol, and solvent contained in the extract is separated in a low boilers still train. Butanol and acetone are recovered in pure form in this train, whereas crude ethanol is sent to the raffinate train for purification. Solvent is separated from lower boiling wastes in the high boilers still and recycled to the extractor.

One potential problem with the use of a high-boiling solvent must be noted. If the solubility of solvent in water is high enough, the loss of solvent to the aqueous waste leaving the process as the tails from the first raffinate still might be unacceptable. A solubility of 20 ppm was assumed in this study. Blanch assumed 100 ppm in his study. Either would be satisfactory.

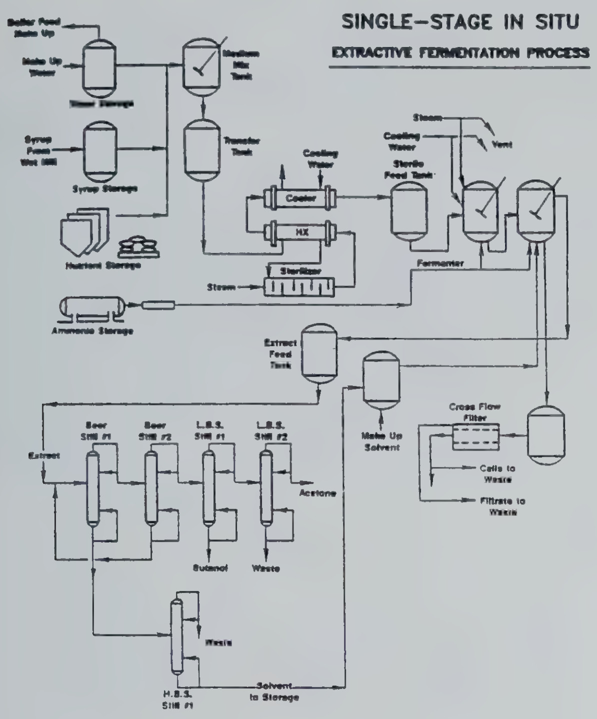
6.2 Process Scenario for In Situ Extraction

The flowsheet for the in situ case is substantially the same as for the external extractor case except that extraction is carried out in the fermenter and no additional extraction vessel is required. Also, aqueous raffinate containing cell debris and unextracted product and by-products is sent to waste disposal. The evaluation of this case did not include the recovery of chemicals in the raffinate. This would probably be justified; in which case the raffinate still train used for the external extractor case would be added. The process is shown in figure 41.



Process Model Used in Economic Study

Figure 40



PROCESS MODEL USED IN ECONOMIC STUDY

NO RECOVERY OF RAFFINATE CHEMICALS

Figure 41
(See page 133d
for enlarged view)

7. Operating Conditions

It was assumed that the plant would be sited in the Midwest adjoining a wet corn mill with dilute 45% syrup supplied over the fence by pipeline. Capacity was sized to a 180 million pound per year butanol plant with a midpoint of construction in 1984 and operating in 1988 at a 160 million pound per year production rate. Technical and financial data for the cases evaluated are provided in the appendixes.

Basic data for the external extraction process are outlined in Table 61 according to whether they are independent or dependent variables. Key equipment dimensions are shown to provide a feeling for scale of the operation. The basecase data for fermentation without cell recycle were obtained from the literature sources discussed earlier. Distribution coefficients were determined by Battelle [60]. A comparison with the basis used by Blanch is as follows:

	This Study	Blanch
Product Concentration, g/l	13.0	13.7
Fermentation Time, hours	33	30
Cell Density, g/l	1.4	3.0
Specific Productivity, g/g*	0.28	--
Volumetric Productivity, g/	0.39	0.46–0.89
Distribution Coefficient		
Butanol	4.3	2.6
Acetone	0.5	0.3
Ethanol	0.2	0.1
Acetic Acid	0.2	n.a.
Butyric Acid	0.2	n.a.

The main differences among cases were whether or not raffinate with cells was recycled and whether raffinate chemicals were recovered. As can be noted from the selling prices required to provide an adequate return on investment, the recycle of cells to the highest operable density is of utmost importance. Recovery of raffinate chemicals is also justified.

Table 61

PROCESS BASIC DATA					
Model Stoichiometry	GOAL	BASE	BASE	BASE	BASE
With Recycle of Raffinate/Cells	yes	yes	yes	no	no
With Recovery of Raffinate Chemicals	n.a.	yes	no	yes	no
Butanol Cost+Return Selling Price, $/lb	0.35	0.43	0.48	1.07	1.05
Specified Operating Parameters					
Annual Capacity, Million lb/yr			180		
Butanol Cencentration in Beer, g/l			13		
Specific Productivity, g BuOH/g cells*hr			0.283		
Glucose to Products, % of converted			95%		
Solvent to Beer Ratio			0.3		
Butanol Yield to Extract, lb/lb in beer	0.970	0.970	0.970	0.999	0.999
Raffinate & Cell Recycle Ratio	27:1	15:1	15:1	-0-	-0-
Dependent Variables					
Glucose Demand, lb/lb butanol	2.56	4.29	4.29	4.29	4.29
Cell Density, g/l	21.1	21.8	21.8	1.4	1.4
Dilution Rate, l/hr	0.46	0.48	0.48	0.03	0.03
Volumetric Productivity, g BuOH/l*hr	6.0	6.2	6.2	0.4	0.4
Butanol Yield Across Refining, % fed	99.4	98.8	98.8	98.9	98.9
Fermenter Volume, 1000 gal (gross)	635	616	616	9654	9654
Extractors - Stages	9	9	9	20	20
- Height, ft	28	28	28	50	50
- Diameter, ft	11.5	11.5	11.5	11.1	11.1
- number	4	4	4	4	4
Beer Still #1 - Plates	11	10	10	10	10
- Height, ft	31	30	30	30	30
- Diameter, ft	5.4	6.4	6.4	5.8	5.8
Raffinate Still #1 - Plates	n.a.	32	--	42	--
- Height, ft	n.a.	63	--	78	--
- Diameter, ft	n.a.	4.9	--	18.9	--

Data used for the in situ extraction case are the same as the above except that no recycle or raffinate recovery was involved.

8. Extraction Performance

In continuous, multistage, countercurrent extraction a trade-off must be made between the required number of stages, which determines the cost of the extractor, and the solvent-to-aqueous feed ratio, which determines the cost of recovering product from the solvent extract. The number of stages required for the separation approaches infinity as the product of the distribution coefficient times the solvent/feed ratio approaches unity. As a practical matter, this product should be controlled fairly close to unity for a proper balance.

For the external extractor basecase, a solvent/feed ratio of 0.3 at a distribution coefficient of 4.3 ($0.3 \times 4.3 = 1.29$) called for 9 stages at a yield of 97%. As will be discussed later, this combination appeared to provide the lowest cost. The yields of acetone (15%) and ethanol (6%) are low because of their low distribution coefficients and low solvent/feed ratio.

For the in situ extraction case, the fermenter acts as a single stage of extraction. Consequently, the efficiency is lower than for the multistage case, but much higher effective concentrations of product in the fermenter can be realized.

Yields of product to extract for single-stage extraction for various distribution coefficients and solvent/beer ratios are shown in figure 42. At a distribution coefficient of 4.3, a solvent/beer ratio of 3.5 would lead to a distribution of 93.8% of the butanol solute in the fermenter to the extract. At its lower distribution coefficient, the yield of acetone to extract would be about 60%, and the yield of ethanol, 40%.

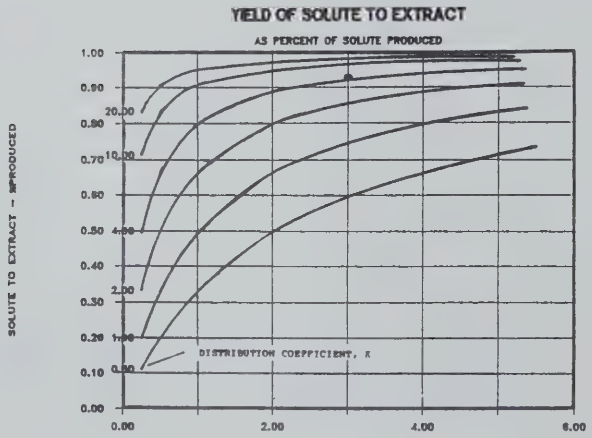


Figure 42

The improvement possible in effective concentration is shown in figure 43 in which "initial" concentration represents the amount of product produced relative to the aqueous flow. Thus at a solvent/feed of 3.5, the effective concentration of product in the fermenter can be increased to close to 200 g/l while maintaining the actual concentration in the aqueous raffinate (beer) at 13 g/l, the threshold of inhibition.

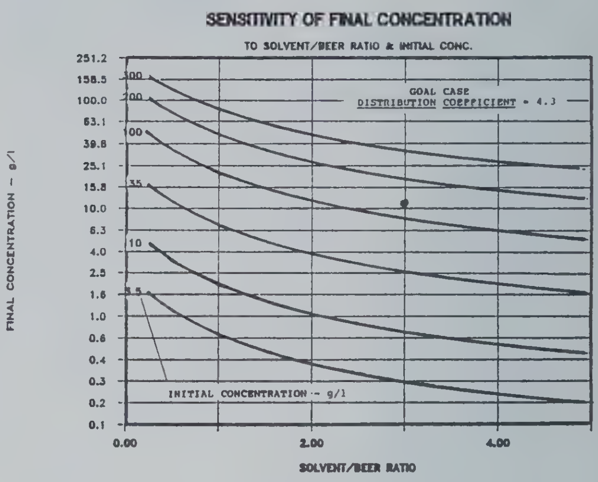


Figure 43

It should be noted that although oleyl alcohol was used as a model solvent in this study, as well as many others reported in the literature, it could not be used in commercial practice since it boils too high to allow a practical separation of product from the extract. It was assumed in this study that the oleyl alcohol was either in a carrier of nonyl alcohol or that a new solvent was identified that had the solvent characteristics of oleyl alcohol and the distillation characteristics of nonyl alcohol.

9. Projected Economics of Conventional Weizmann Process

Butanol currently sells for $0.38 per pound at a crude oil price of $15-$20 per barrel. This price has been fairly stable since 1982. However, considering the increases expected again in crude oil prices in the 1990's, a doubling in the price for oil-based butanol is not inconceivable.

Lenz and Moreira analyzed the economics of the conventional Weizmann process utilizing a molasses substrate and found that the process would have to operate at a loss because of the combined effect of raw material costs and dilute concentrations [62].

The current study also concluded that the Weizmann process would operate at a loss in the present economic environment. Butanol from a 170 million pound per year plant based on the conventional process and operating at 150 million pounds per year in 1987 would cost about $1.19 per pound for the fermentation operation alone (including raw materials cost but excluding recovery and purification costs) [63]. This cost includes a 30% pretax return on investment.

The investment at a midpoint of construction of 1983 is comprised of: $230 million in direct process equipment; $33 million in allocated power, services and general facilities; and $30 million in working capital. Of the direct process investment, $200 million alone is for fermenters (16 million gallons) and their ancillaries priced installed at $12.50 per gross gallon. A contingency factor of 30% was applied to the investment. Working capital is high because of the high value of the product inventory and accounts receivables.

This estimate assumes a butanol concentration of 13 g/l at a batch time of 40 hours and a turnaround of 12 hours. Of the glucose converted, 5% is used for cell growth and 95% for products according to the stoichiometry of Table 60. The product cost sheet is summarized as follows:

Raw Materials	$0.30
Utilities	$0.04
Labor Related	$0.03
Depreciation	$0.14
Other Capital Related	$0.05
Cost of Manufacture	$0.56
SE, R&D, Administration	$0.16
Cost of Sales	$0.72
Pretax Earnings	$0.58
By-product Credit	($0.11)
Cost-Plus-Return Price	$1.19

Wang compared the economics of extractive batch fermenter designs with conventional batch designs and concluded that the extraction design appeared to be considerably more profitable than the conventional design [64]. Blanch reached a similar conclusion with respect to a fed-batch extractive design [65].

10. Projected Economics of External Extraction Process

External multistage extraction combined with raffinate/cell recycle and recovery of chemicals in the raffinate appears to have a dramatic effect on reducing product costs. For the first time in over 30 years it now seems that the fermentation process is within striking distance of competing with synthetic butanol at $0.38 per pound. The economics of the five cases developed for the external extraction process are summarized in Table 62. The mandatory prices are based on attaining a pretax return on investment of 30%.

With a 15:1 recycle and recovery of raffinate chemicals the cost-plus-return price appears to be reduced to $0.43 per pound. With a double recycle and higher recycle ratio further reductions appear possible, although these may be marginal.

The development of organisms that are less inhibited by product and/or have a selective stoichiometry favoring the production of butanol appears to reduce cost below the present price for synthetic butanol.

These conclusions will be discussed further in the following sections.

10.1 Effect of Raffinate/Cell Recycle

Cost is primarily sensitive to the recycle of cells. As shown in Table 63, cost decreases with increases in recycle ratio over the entire range studied. This effect mainly results from a concomitant reduction in fermenter and total plant investment. For this model, recycle ratios over 15:1 would require evaporation of the syrup—an undesirable requirement. However this could be avoided by using a double recycle if cell concentrations above 22 g/l could be tolerated in the fermenter. Total flow through the fermenter remains constant irrespective of recycle ratio for a fixed, limiting product concentration and annual production rate. Cell density increases as cell recycle increases; so that fermentation time and fermenter investment can be decreased correspondingly to balance production rate at a constant specific productivity.

10.2 Effect of Solvent/Beer Ratio

The solvent to beer ratio should be minimized for optimum costs. The cost trade-off of operating parameters is shown in Table 64. For the conditions of this study the best ratio appears to be 0.3. For a distribution coefficient of 4.3, the plates required in the extractor approach infinity at a ratio of 0.23, but drop sharply to reasonable levels at slightly higher ratios. As solvent/beer ratio increases, the number of extractor stages that are required decreases but throughput and, hence, extractor diameter and/or number increase. These opposing effects modulate extractor investment. However, both distillation and steam investment increase in order to process the higher volume of fluid downstream.

Table 62

EXTRACTIVE FERMENTATION OF BUTANOL
MULTISTAGE EXTERNAL EXTRACTION
(Production Level - 160 Million PPY)

Stoichiometry	Base	Base	Base	Base	Goal
Raff/Cell Recycle	15:1	15:1	0	0	26:1
Recover Chemicals	Yes	No	Yes	No	n.a.
INVESTMENT-$MILLION					
MPC = 1984					
Direct Permanent Investment	$27.3	$25.8	$170.7	$159.3	$20.1
Allocated Power, Services & General	$12.9	$10.6	$60.0	$34.9	$8.2
Working Capital	$14.4	$15.1	$26.9	$25.5	$10.1
Total Investment	$54.5	$51.6	$257.5	$219.7	$38.4
COST-$/LB (1988)					
Raw Materials	$0.29	$0.29	$0.29	$0.29	$0.17
Utilities	$0.04	$0.04	$0.11	$0.07	$0.02
Labor-Related	$0.03	$0.03	$0.03	$0.03	$0.03
Capital-Related	$0.02	$0.02	$0.15	$0.13	$0.02
Cost of Manufacture	$0.38	$0.38	$0.57	$0.52	$0.24
SE, D, R&D, Adm, & I.C.	$0.05	$0.06	$0.14	$0.13	$0.05
Cost of Sales	$0.44	$0.44	$0.71	$0.65	$0.28
Pretax Earnings Based on: 30% Pretax ROI	$0.10	$0.10	$0.48	$0.41	$0.07
By-product Credit	($0.11)	($0.06)	($0.11)	($0.01)	($.00)
Selling Price	$0.43	$0.48	$1.07	$1.05	$0.35

Table 63

SENSITIVITY ANALYSIS
EFFECT OF RECYCLE RATIO ON FERMENTATION PERFORMANCE

For K=4.3; Solvent/Feed Ratio=0.3
Product Concentration=13 g/l; Specific Productivity=0.283 g/g*h

RECYCLE RATIO	COST $/lb	TPI $million	FERMENTER $million	CELLS g/l	DILUTION RATE,l/hr	VOL.PROD g/l*hr
0.0	$1.078	$228	$117	1.4	0.030	0.39
0.5	$0.854	$164	$78	2.1	0.045	0.59
1.0	$0.741	$132	$59	2.8	0.060	0.78
2.0	$0.626	$98	$39	4.2	0.090	1.18
4.0	$0.533	$71	$24	6.9	0.151	1.96
6.0	$0.491	$59	$17	9.7	0.211	2.74
8.0	$0.468	$52	$13	12.5	0.272	3.53
10.0	$0.452	$48	$11	15.3	0.332	4.32
12.0	$0.441	$44	$9	18.1	0.393	5.11
14.0	$0.433	$42	$8	20.9	0.454	5.90
15.0	$0.430	$41	$7	22.3	0.484	6.30

Table 64

SENSITIVITY ANALYSIS
EFFECT OF SOLVENT/BEER RATIO ON FERMENTATION PERFORMANCE

For K=4.3; Recycle Ratio=15; Extract Yield=99.0%
Product Concentration=13 g/l; Specific Productivity=0.283 g/g*hr
Cell Density=22.3 g/l, Volumetric Productivity=6.3 g/l*hr

SOLVENT/ WATER	COST $/lb	TPI $million	STILLS $million	STEAM $million	EXTRACTORS $million	STAGES	DIAM-ft	NUMBER
0.30	$0.430	$41.0	$5.5	$8.1	$5.5	13	11.5	4
0.40	$0.434	$41.5	$5.9	$9.7	$3.9	7	11.9	4
0.50	$0.444	$43.8	$6.3	$11.2	$4.0	6	11.0	5
0.75	$0.468	$48.8	$7.2	$15.2	$3.7	4	11.6	5
1.00	$0.492	$54.3	$8.2	$19.1	$3.8	3	11.4	6
1.50	$0.544	$66.0	$10.1	$26.9	$4.6	3	11.8	7
2.00	$0.597	$77.9	$12.1	$34.6	$5.7	3	11.3	9
2.50	$0.647	$88.9	$14.1	$42.4	$5.7	2	11.6	10
3.00	$0.700	$100.7	$16.2	$50.2	$6.5	2	11.8	11

10.3 Effect of Extractor Yield

A similar trade-off occurs in the choice of yield of product to extract. As yield increases, so does the number of stages required to effect the separation, in opposition to the improvement in process efficiency. As shown in Table 65, a cost optimum in reached at a yield of about 97%. Above this, cost rises sharply. If cells are not recycled the optimum would occur at a higher yield.

10.4 Effect of Product Concentration

The basecases of this study were developed on the use of a 13 g/l product concentration—supposedly close to the acceptable limit of feedback inhibition. Lower and higher concentrations were also explored. Higher concentrations would require developing an organism that is less sensitive to product inhibition. This appears to be a worthwhile research goal. The results are summarized in Table 66. Note that dilution rate is synonymous with raffinate recycle ratio.

Table 65

SENSITIVITY OF PRODUCT COST
TO YIELD TO EXTRACT AND SOLVENT/BEER RATIO

	15:1 RAFFINATE RECYCLE		NO RECYCLE	
S/B RATIO:	0.3	0.4	0.3	0.4
YIELD, lb/lb fed				
0.85	$0.440	$0.450	$1.236	$1.250
0.90	$0.434	$0.443	$1.172	$1.183
0.93	$0.430	$0.440	$1.137	$1.148
0.95	$0.429	$0.438	$1.116	$1.126
0.96	$0.428	$0.437	$1.105	$1.115
0.97	$0.428	$0.435	$1.095	$1.104
0.98	$0.428	$0.434	$1.085	$1.094
0.99	$0.430	$0.434	$1.078	$1.085
0.999	$0.436	$0.438	$1.075	$1.080
0.9999	---	$0.442	---	$1.083

Table 66

SENSITIVITY OF FERMENTATION PERFORMANCE
TO PRODUCT CONCENTRATION

(With Recovery of Raffinate Chemicals)

PRODUCT CONC.-g/l	BuOH COST $/lb	TPI $/lb	FERM INV $/lb	FERM INV /TPI	CELLS g/l	DIL RATE 1/hr
		For No Raffinate/Cell Recycle				
3	$3.51	$5.18	$2.91	56%	0.3	0.03
6	$1.94	$2.66	$1.46	55%	0.6	0.03
13	$1.10	$1.30	$0.67	52%	1.4	0.03
18	$0.89	$0.97	$0.49	50%	1.9	0.03
25	$0.74	$0.73	$0.35	48%	2.7	0.03
50	$0.55	$0.41	$0.17	42%	5.4	0.03
100	$0.45	$0.25	$0.09	35%	10.7	0.03
		For 0.5:1 Raffinate/Cell Recycle				
3	$2.53	$3.60	$1.94	54%	0.5	0.05
6	$1.45	$1.87	$0.97	52%	1.0	0.05
13	$0.87	$0.93	$0.45	48%	2.1	0.05
18	$0.72	$0.70	$0.32	46%	2.9	0.05
25	$0.62	$0.53	$0.23	44%	4.0	0.05
50	$0.48	$0.31	$0.12	37%	8.0	0.05
100	$0.41	$0.20	$0.06	30%	15.9	0.05
		For 2:1 Raffinate/Cell Recycle				
3	$1.56	$2.02	$0.97	48%	0.9	0.09
6	$0.96	$1.07	$0.49	45%	1.9	0.09
13	$0.63	$0.55	$0.22	41%	4.1	0.09
18	$0.55	$0.42	$0.16	38%	5.7	0.09
25	$0.49	$0.33	$0.12	35%	7.9	0.09
50	$0.42	$0.21	$0.06	28%	15.8	0.09
100	$0.38	$0.14	$0.03	21%	31.8	0.09
		For 5:1 Raffinate/Cell Recycle				
3	$1.07	$1.22	$0.49	40%	1.9	0.18
6	$0.71	$0.66	$0.24	37%	3.8	0.18
13	$0.51	$0.36	$0.11	32%	8.2	0.18
18	$0.46	$0.28	$0.08	29%	11.3	0.18
25	$0.43	$0.22	$0.06	26%	15.8	0.18
50	$0.38	$0.15	$0.03	20%	31.7	0.18
100	$0.36	$0.11	$0.02	14%	64.0	0.18
		For 10:1 Raffinate/Cell Recycle				
3	$0.84	$0.85	$0.26	31%	3.4	0.32
6	$0.59	$0.47	$0.13	28%	6.9	0.33
13	$0.45	$0.26	$0.06	24%	15.0	0.33
18	$0.42	$0.21	$0.04	21%	20.8	0.33
25	$0.40	$0.17	$0.03	19%	29.0	0.33
50	$0.37	$0.12	$0.02	13%	58.6	0.33
100	$0.36	$0.09	$0.009	9%	119.6	0.34
		For 15:1 Raffinate/Cell Recycle				
3	$0.75	$0.70	$0.18	26%	5.0	0.47
6	$0.54	$0.39	$0.09	23%	10.0	0.47
13	$0.43	$0.22	$0.04	19%	21.8	0.48
18	$0.40	$0.18	$0.03	17%	30.3	0.48
25	$0.38	$0.15	$0.02	15%	42.3	0.48
50	$0.36	$0.11	$0.01	10%	86.0	0.49
100	$0.36	$0.09	$0.006	7%	177.7	0.50

At any product concentration it is clearly desirable to operate at as high a recycle ratio (dilution rate) as possible. At 13 g/l and a 15:1 ratio, cell density would reach 22 g/l. This level appears operable, but densities required for concentrations above, say, 50 g/l (even if attainable without inhibition) may produce unacceptable viscosities and adverse effects on the organism in the fermenter. As a practical matter, it does not appear that increasing concentration much above 25 g/l will have a significant effect on reducing further the cost of the product.

It can also be noted that at a 15:1 ratio (0.48 hr^{-1} dilution rate) the cost curve is close to the "infinite" dilution rate curve at which point further decreases in fermenter volume have an insignificant effect on cost and investment.

10.5 Effect of Sugar Price and Yield

The cost of the sugar substrate is a very important element of cost; particularly if the engineering improvements discussed in previous section can be realized. For Basecase A, the cost of substrate amounts to 65% of the $0.43 per pound selling price and 74% of the cost of manufacture. This cost combines the effects of sugar price and yield to product.

If an organism can be developed to provide the stoichiometry indicated as the goal case of Table 54, the cost-plus-return selling price could be reduced from $0.43 per pound to $0.35 per pound, i.e., below the current price for synthetic butanol. This case is summarized in Table 56.

The study was based on the availability of a contract supply of a dilute 45% corn syrup from an adjoining wet mill at a transfer price of $0.065 per pound equivalent glucose. The sensitivity of butanol cost to sugar price is shown in figure 44. If sugar were free, cost-plus-return would drop to $0.09 per pound.

Commercial acceptance of the enhanced fermentation process will ultimately depend on the direction taken by crude oil prices. This market is still soft at about $17-$20 per barrel. However, a doubling of the $0.38 price for butanol over the next decade is not out of the question.

10.6 Effect of Recovery of Raffinate Chemicals

Since butanol is the primary product of the ABE system, the process model was designed to extract substantially all of it with a reasonable number of extraction stages. However, since the major

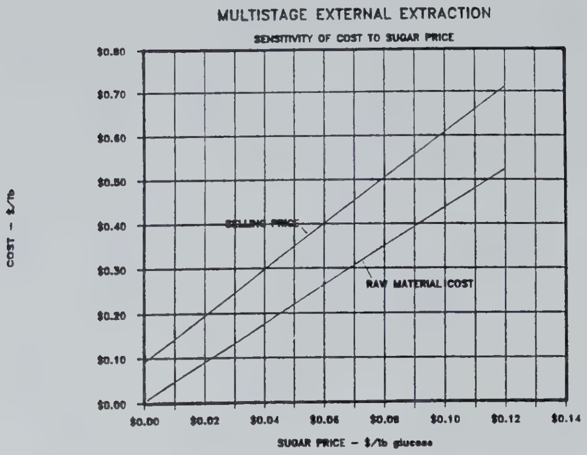


Figure 44

by-products: acetone and ethanol have lower distribution coefficients, a considerable portion of that which is produced remains in the aqueous raffinate. For this system it appears that the recovery of these by-products from the raffinate purge is economically justified provided that raffinate and cells are recycled at the level studied. Indeed, the return on the additional investment required amounts to 220%. The cases with and without recovery compare as follows:

Expense – $/lb	No Recovery	Recovery	Difference
Cost of Sales	$0.444	$0.439	($0.005)
Acetone Credit	($0.062)	($0.084)	($0.022)
Ethanol Credit	$0.000	($0.028)	($0.028)
Total	$0.382	$0.327	($0.055)
Investment – $/annual lb			
New Stills	$0.000	$0.009	$0.009
By-product Storage	$0.004	$0.008	$0.004
Steam	$0.035	$0.045	$0.010
Sub Total	$0.039	$0.062	$0.023
Total Plant Investment	$0.203	$0.228	$0.025 *

* $4.5 million for 180 MM PPY plant
Return on Additional Investment = $0.055/$0.025 = 220%

11. Projected Economics of In Situ Extraction Process

The cost-plus-return for butanol as manufactured by the in situ extraction model would amount to $0.49 per pound at the same 22 g/l cell density as for the external extraction case, for which the cost was $0.48 per pound without recovery of raffinate chemicals. Both models would benefit further by recovery of the by-products, but that scheme was not included in the in situ model. As with the external extractor case, the minimum cost of the in situ case depends on the extent to which cell density can be increased. In the case of the in situ basecase, increasing the solvent to feed ratio at a fixed dilution rate is the main operating approach. A basecase ratio of 3.5 at a 0.03 hr^{-1} dilution rate was used here. A summary of the economic picture is provided in Table 67.

Table 67

```
       SINGLE-STAGE INSITU EXTRACTIVE FERMENTATION OF BUTANOL
                 NO RECOVERY OF RAFFINATE CHEMICALS
                      BASECASE STOICHIOMETRY
                             SUMMARY
                             -------
                                                   PRODUCTION LEVEL
                                                       163   MM PPY
                                                   ----------------
INVESTMENT-$MILLION
    MPC = 1984
------------------------------
    Direct Permanent Investment                           $21.6
    Allocated Power, Services & General                    $9.5
    Working Capital                                       $15.8
                                                          -----
          Total Investment                                $47.0

COST-$/LB ( 1988 )
------------------
    Raw Materials                                         $0.30
    Utilities                                             $0.05
    Labor-Related                                         $0.03
    Capital-Related                                       $0.02
                                                          -----
        Cost of Manufacture                               $0.40
    SE, D, R&D, Adm, & I.C.                               $0.06
                                                          -----
        Cost of Sales                                     $0.46
    Pretax Earnings Based on: 30% Pretax ROI              $0.09
    By-product Credit                                    ($0.06)
                                                          -----
        Selling Price                                     $0.49

FINANCIAL CRITERIA
------------------
    Net ROI 3rd Year (assumed)                              16%
    Investors Rate of Return (20 Operating Years)           17%

    Year to Break Even - Annual Cash                       1987
                       - Cumulative Cash                   1991
                       - Cum. Disc. Cash (NPV)             1995

    Net Present Value $MM (20 years @ 12%)                $16.4
```

11.1 Effect of Solvent/Feed Ratio

Cost is reduced by raising the solvent to feed ratio to the highest level possible. As noted in Table 68, cost might be reduced to $0.39 per pound at a 20:1 ratio if a cell density of 120 g/l were operable, but that seems doubtful. A large portion of the saving is related to the reduction in fermenter volume and investment that results from the trade-off with cell density at constant specific productivity. At high solvent/feed ratios fermenter investment becomes insignificant compared with total plant investment and in effect an "infinite" ratio is reached.

Table 68

INSITU EXTRACTIVE FERMENTATION
EFFECT OF SOLVENT/FEED RATIO ON FERMENTATION PERFORMANCE

For K=4.3; Product Concentration=13 g/l
Specific Productivity=0.283 g/g*hr

SOLVENT/ FEED	COST $/lb	TPI $million	FERMENTER $million	EFF PROD CONC-g/l	CELLS g/l	DILUTION RATE, l/hr	VOL PROD g/l*hr
0.25	$1.442	$105	$70	27	3	0.03	0.8
0.50	$0.958	$78	$46	41	4	0.03	1.2
1.00	$0.702	$56	$28	69	7	0.03	2.1
2.00	$0.560	$40	$15	125	13	0.03	3.8
3.00	$0.507	$33	$11	181	19	0.03	5.5
4.00	$0.479	$30	$8	237	25	0.03	7.2
5.00	$0.460	$27	$7	292	31	0.03	8.9
7.00	$0.437	$24	$5	404	43	0.03	12.3
10.00	$0.419	$22	$3	572	61	0.03	17.3
15.00	$0.403	$20	$2	851	91	0.03	25.8
20.00	$0.394	$18	$2	1131	121	0.03	34.3

Distribution coefficient is an important adjunct to solvent/feed ratio. This effect is shown in figure 45. If a coefficient of 4.3 cannot be attained in commercial operation, the reduction in performance can be compensated for to some extent by raising the ratio.

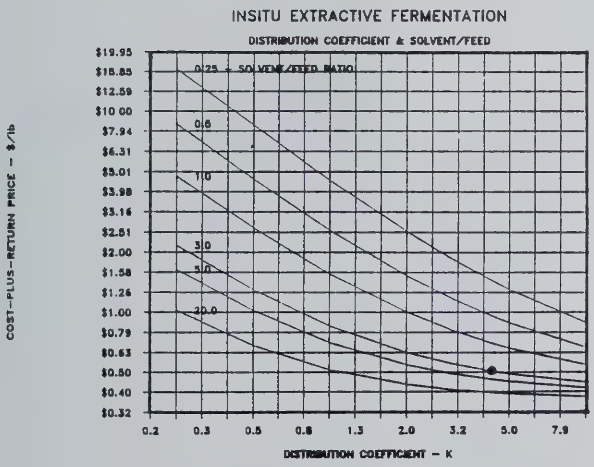


Figure 45

11.2 Effect of Butanol Concentration

For the in situ evaluation, butanol concentration was held constant at 13 g/l, the threshold of inhibition for the existing organism. However cost performance could be improved if product inhibition could be reduced. The effect of increasing the allowable concentration in conjunction with changes in solvent/feed ratio is shown in figure 46.

Similarly, cost could be reduced by developing a more active organism with a higher specific productivity that could operate at a dilution rate higher than the 0.03 hr^{-1} used in the in situ base-case. The combined effect of improvements in both dilution rate and product concentration is shown in figure 47. Data for an "infinite" dilution rate are included. That curve represents the limit to which the fermenter performance can be pushed.

11.3 Effect of Sugar Price

As might be expected, cost is highly sensitive to sugar price. This effect is shown in figure 48. It will be very important to the viability of either extraction mode to provide a cost effective supply of syrup to the commercial venture.

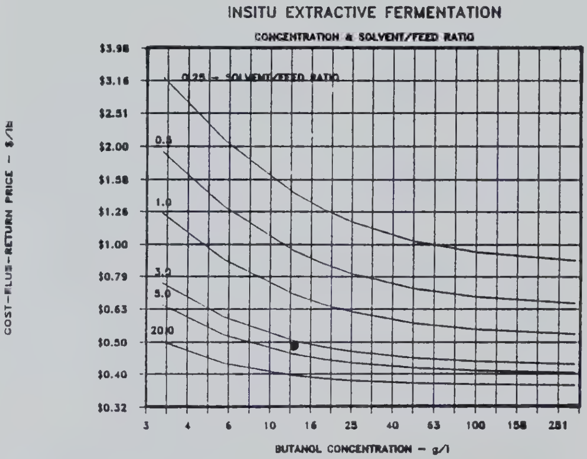


Figure 46

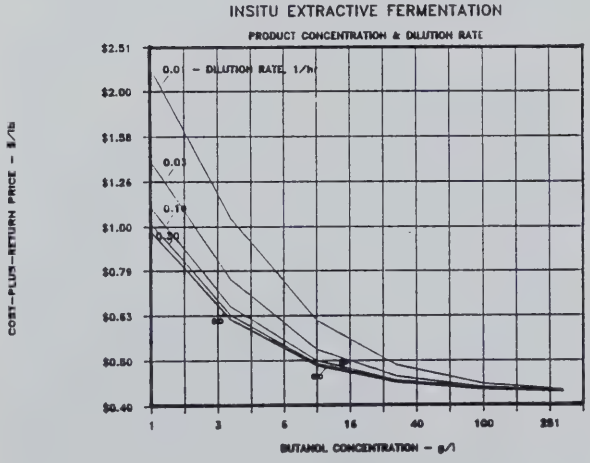


Figure 47

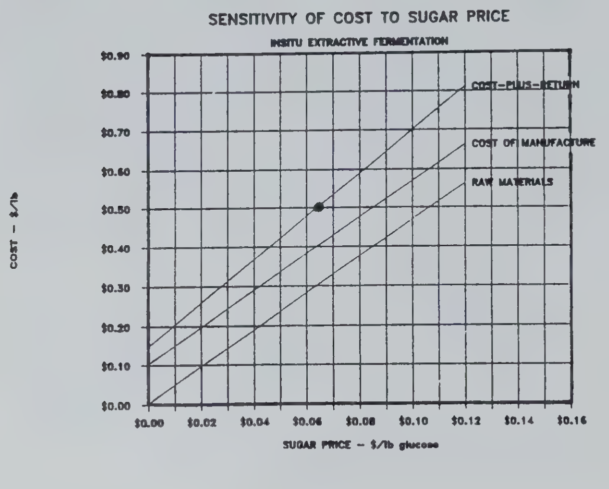


Figure 48

12. Recommendations

It appeared from the results of the study that either the external or in situ extraction processes would be equally effective in reducing the cost of producing butanol to commercially acceptable levels. However, the external process would appear to be more easy to develop and operate on a commercial scale. Accordingly, the following recommendations are made as a guide to further research in this area:

(1) Demonstrate continuous operation of the fermentation process on a rack or pilot scale over an extended run time, say, 1000 hours.

(2) Immobilize the cells and/or add a crossflow filter or similar separation device so as to retain the cells in the fermenter or recycle them to the desired maximum cell density while increasing flow through the fermenter to hold product concentration at its optimum level relative to feedback inhibition.

(3) In a separate system, test the continuous countercurrent extraction of butanol, acetone, and ethanol by oleyl alcohol or an improved solvent using a synthetic beer that mimics the expected impurity and salt levels of the fermentation beer (or use the actual beer if such is available at that time).

(4) Concurrently, in a separate small scale laboratory study, seek a solvent having better distillation characteristics than oleyl alcohol with at least the same distribution coefficient and low toxicity. A solvent boiling below water might be considered. Although this would require a different process scenario than the one used in this study for a high boiling solvent, it might offer advantages over the high boiling recovery process. In the selection of a new solvent, attention should be paid to the following potential problems: (a) separation of high boiling acids, if any are present and at a sufficiently low pH to be extractable, might be difficult; (b) if the solubility of water in the solvent is much higher than the 20 ppm that was assumed, problems with azeotropes in the recovery still train involving acetone, butanol and ethanol could arise; and (c) if the solubility of solvent in water is much higher than the 20 ppm that was assumed, additional investment would be required to recover and/or dispose of solvent in the waste raffinate.

(5) Integrate the fermentation unit with the extraction unit and demonstrate operability without cell retention or recycle, then with cell buildup, and finally with raffinate recycle to assess possible adverse effects from the buildup of unextracted products or toxins.

(6) Consider the concurrent development of a genetically revised organism that produces only butanol as its solvent slate and/or has an enhanced specific productivity.

(7) Continue the comparative evaluation of the economics of both processes as new information is obtained from the research program. In the event a clear preference for the in situ process emerges adapt the experimental program to the direct feed of solvent to the fermenter and demonstrate the in situ process

13. Conclusions

Based on the economic analyses it appears that the extractive fermentation system could substantially reduce the cost of butanol and other similar high boiling fermentation products that are now produced at low product concentrations as a result of product inhibition. Such an economic breakthrough cannot be realized until the system has been fully demonstrated in a continuous process over an extended period at pilot scale, optimized according to the findings of this study, and scaled up for the specific fermentation process of interest.

However there appears to be no inherent design limitation in effecting the engineering improvements required in the process operation.

Such may not be the case in attempting to develop an organism with an improved stoichiometry and/or specific productivity. The goal is sufficiently important, however, to warrant the laboratory effort. Certainly, these improvements would represent major breakthroughs in not only the butanol process, but generically any fermentation process that suffers from product inhibition (which is most of them), particularly where the product boils higher than water.

PART VIII

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PART IX

About the Author

Robert M. Busche received his Doctor of Science degree from Washington University (St. Louis) in 1952 with a thesis on "Kinetics of Powdered Coal Gasification." He joined Dupont at Belle Works developing coal gasification for methanol synthesis after three years as a process engineer in the Fischer-Tropsch plant at the Bureau of Mines Coal-to-Oil Demonstration Branch at Louisiana, MO.

Dr. Busche served 33 years with Dupont in various managerial positions in marketing, research and manufacturing related to synthesis gas manufacture, nylon intermediates, polyolefins, and Teflon* tube heat transfer products. His service included 20 years in the planning and management of research and new venture development in biotechnology for the Life Sciences Division of the Central Research & Development Department. This also involved setting up a new venture in Mycoprotein* meat analogs with Ranks Hovis McDougal and guiding research on the use of renewable resources for manufacturing specialty chemicals and feedstocks.

After retiring from Dupont in 1985, Dr. Busche founded, and is presently president of, Bio En-Gene-Er Associates, Inc.—a group of over 50 technical, business, and legal consultants in the field of biotechnology.

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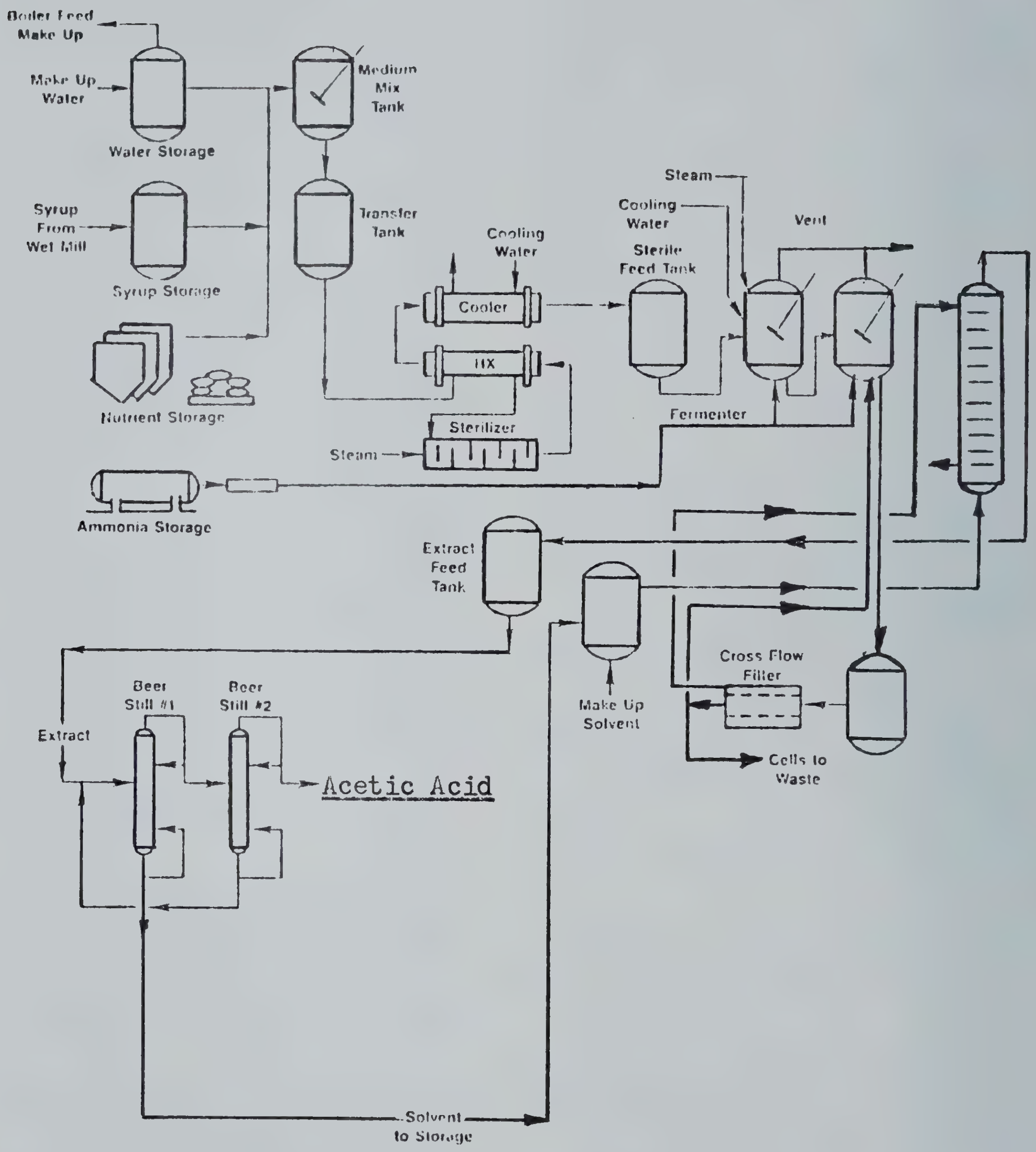

Process Model Used in Economic Study

Figure 35

PROCESS FOR PRODUCING SOLVENTS

BY FERMENTATION OF MOLASSES

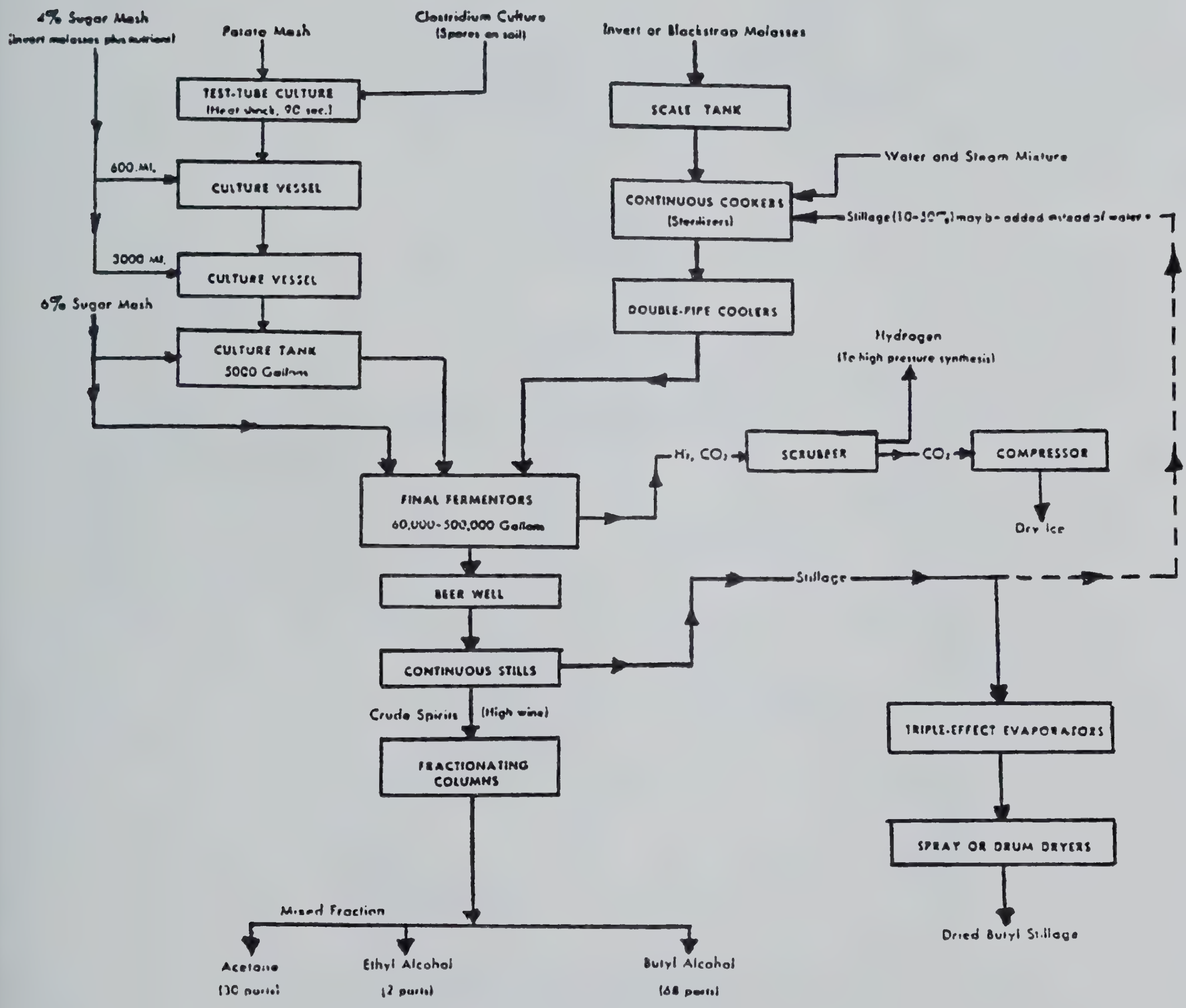

Figure 37. Process for producing solvents.

METABOLIC PATHWAY

GLUCOSE USE BY CLOSTRIDIUM BACTERIA

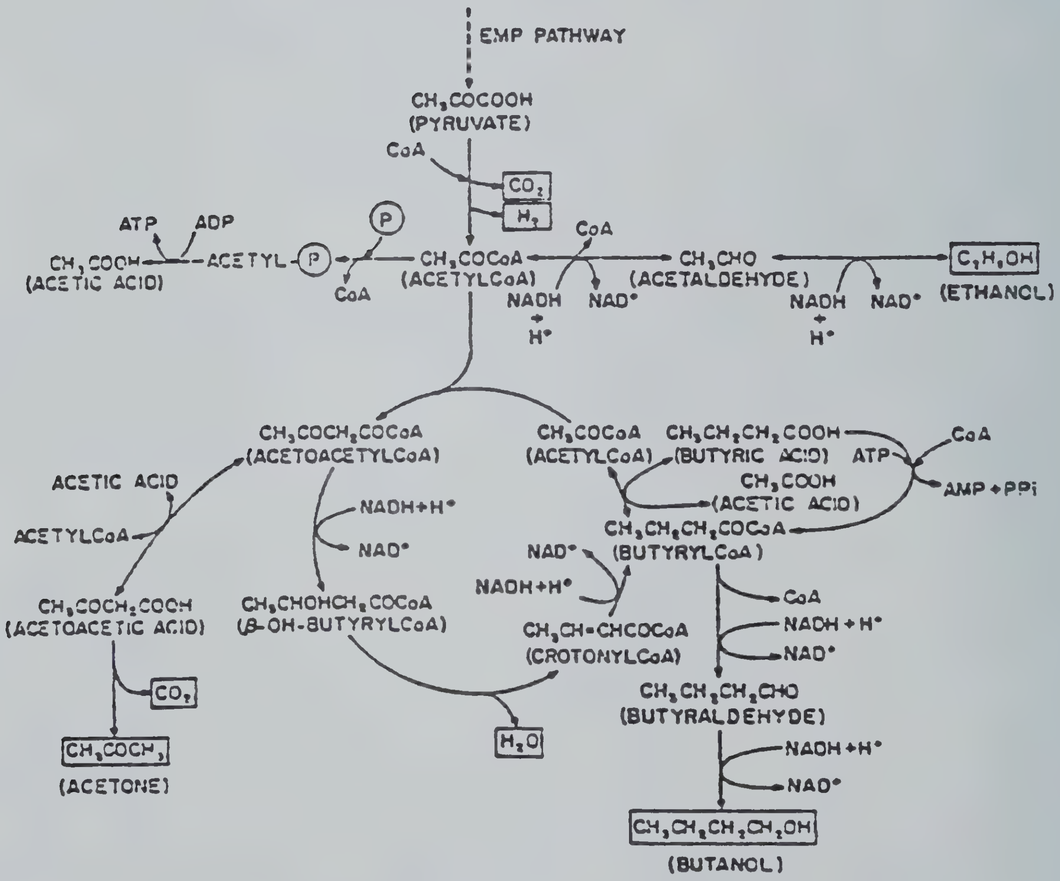

Figure 38. Metabolic pathway—glucose use by clostridium bacteria.

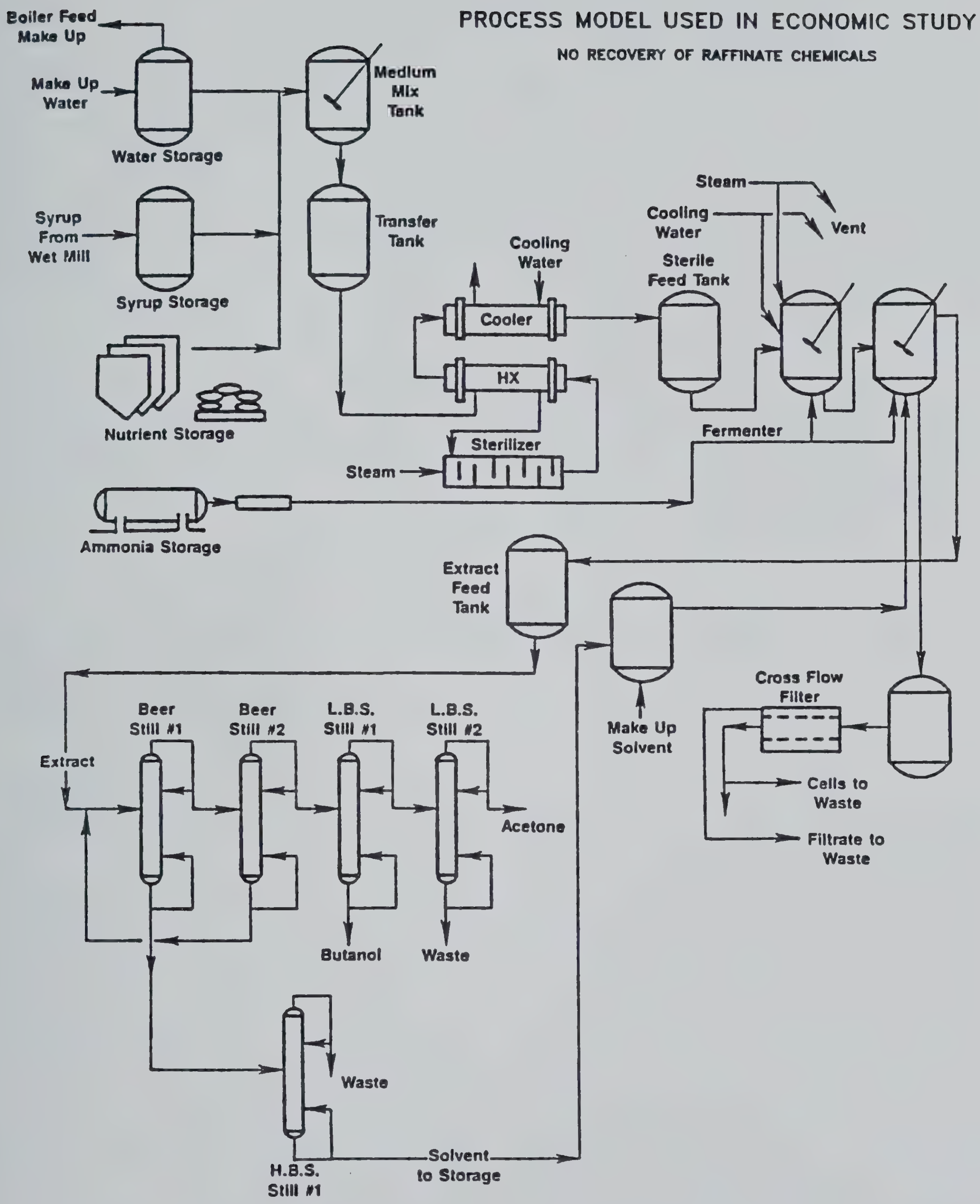

Figure 41. Single-stage in situ extractive fermentation process.

Biodegradable Plastics

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The disposal of plastics in an ecologically sound manner has resulted in the evolution of two new growth industries—Recyclable Plastics and Biodegradable Plastics. The focus of this chapter is on biodegradable plastics. These new plastics are targeted towards single-use, disposable packaging, consumer goods, disposable nonwovens, coatings for paper and paperboard and some non-packaging markets. The growth of composting as an ecologically sound waste management approach supports the need for biodegradable plastics in the market place. Polyesters such as poly(e-caprolactone), poly(lactic acid), poly(hydroxybutyrate-co-hydroxyvalerate), thermoplastic starch and modified starch formulations, poly(vinyl alcohol), and protein polymers, are examples of biodegradable polymeric materials being introduced into the market place. ASTM subcommittee D20.96 has developed Standards in the area of biodegradable plastics.

Key words: ASTM standards; biodegradable; composting; plastic; polyesters; starch.

1. Introduction

Today's plastics are designed with little consideration for their ultimate disposability or recyclability. This has resulted in mounting worldwide concerns over the environmental consequences of such materials when they enter the waste stream after their intended uses. Of particular concern are polymers used in single use, disposable plastic applications. Plastics are strong, light-weight, inexpensive, easily processable and energy efficient. They have excellent barrier properties. They are disposable, and very durable. However, these very attributes of strength and indestructibility cause problems when these materials enter the waste stream. They are not readily broken down by the natural elements in the environment or in waste management infrastructures such as composting to become a part of the biological carbon cycle of our ecosystem. This results in an irreversible build-up of these materials in the environment causing scarring of landscapes, fouling of beaches, and posing a serious hazard to marine life. Plastics are resistant to biological degradation because microorganisms do not have enzymes capable of degrading and utilizing most man made polymers. In addition, the hydrophobic character of plastics inhibits enzyme activity and the low surface area of plastics with their inherent high molecular weight further compounds the problem.

New environmental regulations, societal concerns, and a growing environmental awareness throughout the world have triggered a paradigm shift in industry to develop products and processes compatible with the environment. At the International level under the aegis of the International Standards Organization (ISO) and International Electrotechnical Committee (IEC) a Strategic Advisory Group on the Environment (SAGE) has been created to develop "Environmental Standards." One of the SAGE subgroups on Environmental Labeling was charged with looking at definitions and terminology of environmental terms such as biodegradability, compostability, recyclability, and test methods to substantiate claims for using these terms.

Therefore, there has begun an urgent search to redesign and engineer new polymeric materials that have the needed performance characteristics of plastics, but can be transformed in appropriate waste disposal infrastructures to products that are compatible with the environment, or can be recycled to the same or other products. Thus, the twin issues of recyclability and biodegradability of plastics are becoming very important [1]. It is also important to have appropriate waste management infrastructures that utilize the biodegradability or recyclability attributes of the materials, and insure that these materials end up in the appropriate infrastructure—a "cradle to grave" design for materials that integrates material design concepts with appropriate waste management infrastructure (fig. 49). This leads us to the concept of designing and engineering new biodegradable materials—materials that have the performance characteristics of todays materials, but undergo biodegradation along with other organic waste to soil humic materials (compost). By composting our biodegradable plastic and paper waste along with other "organic" compostable materials like yard, food, and agricultural wastes, we can generate much-needed carbon-rich compost (humic material). Compost amended soil has beneficial effects by increasing soil organic carbon, increasing water and nutrient retention, reducing chemical inputs, and suppressing plant diseases. The problem of waste disposal could become the solution for low-input sustainable agriculture. A significant fraction of the municipal solid waste stream (MSW) is made up of compostable or potentially compostable materials as shown in figure 50.

This chapter:

- Presents the "Cradle to Grave" concept of material design and the role biodegradable plastics play in this concept including which plastics should be targeted for biodegradability
- Shows the rationale for designing fully biodegradable plastic materials in the context of the ecosystem and the biological carbon cycle
- Discusses the role of composting as an important waste management option to transform organic waste to valuable compost for crop applications and the importance of fully biodegradable plastics in compost settings
- Discusses design concepts for biodegradable plastics and the status of the nascent biodegradable materials industry
- Addresses potential markets for biodegradable plastics
- Examines business opportunities in the evolving biodegradable plastics industry

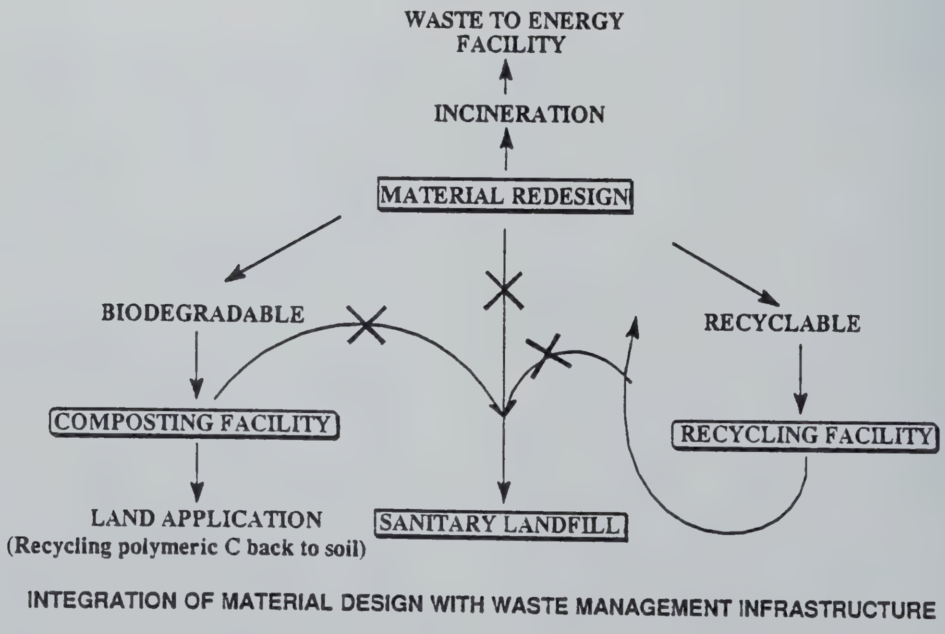

Figure 49. Cradle to grave concept for material design.

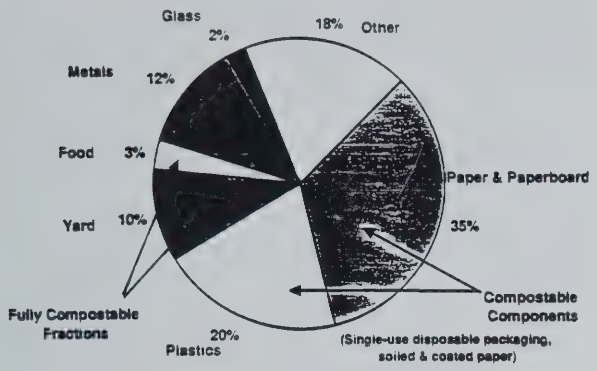

Figure 50. Compostables in MSW by volume.

2. Cradle to Grave Concept of Material Design

As discussed earlier, it is no longer sufficient to design materials with functionality, process efficiency, and economics. The disposal of materials in an ecologically sound manner has become an important factor in the design and use of materials. Therefore, there is a need to design and engineer new materials with recyclability or biodegradability features [1].

There, also, is a need to develop appropriate waste management infrastructures that utilize the recyclability or biodegradability attributes. In addition one has to ensure that the materials end up in the appropriate infrastructure. Recyclable materials need to be collected and sent to a recycling facility to be processed into the same or new products. Biodegradable materials need to be collected and sent to a composting facility so that the materials along with other organic waste undergo biodegradation to soil humic materials (compost). Plowing the resultant compost into agricultural land enhances the productivity of the soil and helps sustain the viability of micro and macro flora and fauna (biological recycling of carbon).

Materials that do not lend themselves to recycling or biodegradation will have to be incinerated with recovery of energy (waste to energy). Landfills are a poor choice as a repository of inert plastic and organic waste. Today's sanitary landfills are plastic-lined tombs designed to retard biodegradation by providing little or no moisture with negligible microbial activity. Organic waste such as lawn and yard waste, paper, food, biodegradable plastics, and other inert materials should not be entombed in such landfills to be "preserved for posterity." Figure 1 shows such a "cradle to grave concept" for material design. The concept involves the integration of materials redesign with appropriate waste disposal infrastructure.

2.1 Disposal of Municipal Solid Waste (MSW)

Figure 50 shows the overall composition of United States municipal solid waste (MSW) stream by volume. Presently, 80% of the municipal solid waste is landfilled. Only 10% is recycled (includes composting) and 10% is incinerated [2]. Yard and food wastes representing 13% by volume are readily biodegradable and should follow the biodegradation-composting pathway shown in figure 49. In recognition of this fact, 17 States in the United States have recently passed legislation that require yard wastes to be composted and have banned these materials from landfills and incinerators. Glass and metals clearly fall into the recyclable category and should follow the recycling pathway of figure 49. Plastics and paper products, representing roughly 50% (54% by volume and 48% by weight) of the MSW stream, do not lend themselves to such ready categorization.

On the basis of technical and economic considerations certain large volume, easily collectable, single resin component plastics, engineering plastics, and composites are recyclable and fit the recycling pathway shown in figure 49. Similarly, clean paper streams such as newsprint, computer paper, and uncoated corrugated containers fit the recycling pathway. However, much of the paper and paperboard products are coated with synthetic polymers (plastics) for barrier properties. These materials along with other single-use, disposable, short-life plastic packaging materials do not readily fit into the recycling or biodegradation pathways shown in figure 49, unless they are designed to be recyclable or compostable.

2.2 Biodegradable Plastics

In line with the "Cradle to Grave" concept of material design not all plastics can and should be made biodegradable. Single-use disposable short-life packaging materials, service ware items (cups, plates, cutlery, etc.), disposable nonwovens (diapers, feminine hygiene products, certain medical plastics), and coatings for paper and paper-board are excellent candidates for biodegradability. Packaging represents the largest market sector for plastics. About 30% of synthetic polymers produced annually are used for packaging applications. Marine plastics such as fishing gear is another category that lends itself to degradable design concepts.

These materials are identified in figure 50 as "compostable components."

Biodegradable plastics should have the needed performance characteristic in their intended use, but after use should undergo biodegradation in appropriate waste management infrastructures to environmentally compatible constituents. For example, a truly biodegradable plastic will be converted to CO_2, H_2O, and compost in a composting infrastructure leaving no persistent or toxic residue.

3. Rationale for Biodegradable Plastics—the Biological Carbon Cycle [3, 4]

Scientists and engineers have developed complex polymeric materials (plastics) with specific and desirable properties from carbon units derived from petrochemical feed stocks. However, the disassembly of these molecules in an ecologically sound manner has been given little attention. Further, the ecological impacts of these plastic materials when they enter the waste stream have not been addressed. The principle law of "Conservation of Mass" tells us that we cannot simply make these man-made materials disappear. However, we can transform them in a proven ecologically sound manner by ensuring that they become an integral part of the biological carbon cycle.

The biological carbon cycle is a process by which the ecosystem cycles organic carbon between various reservoirs: atmosphere, plant and animal substrates (including humans), soil, and micro and macroorganisms. Figure 51 illustrates the biological carbon cycle. Carbon in the form of atmospheric CO_2 is taken up by plants and reduced to carbohydrates (primarily sucrose and starch) by photosynthesis. The carbon in plants is redistributed into herbivorous animals and then into carnivores (secondary recycling of carbon similar to recycling of plastic products into other products). All of these carbon based materials (plants, trees, and all living creatures) are inherently biodegradable, and ultimately result in the formation of dead organic matter. The dead organic matter is decomposed by soil microorganisms in a reversal of the photosynthetic process. Oxygen functions as the most common electron acceptor in the decomposition process. The degradation products serve as carbon and nitrogen sources for the microorganisms. CO_2 and H_2O are produced and a portion of the decomposing substrate is used to form new cell mass. Phenolic components from lignin degradation and microbial synthesis undergo condensation polymerization with protein degradation products resulting in the formation of humic substances [5]. These humic substances degrade much slower and represent a stable, slow-release form of carbon and nitrogen.

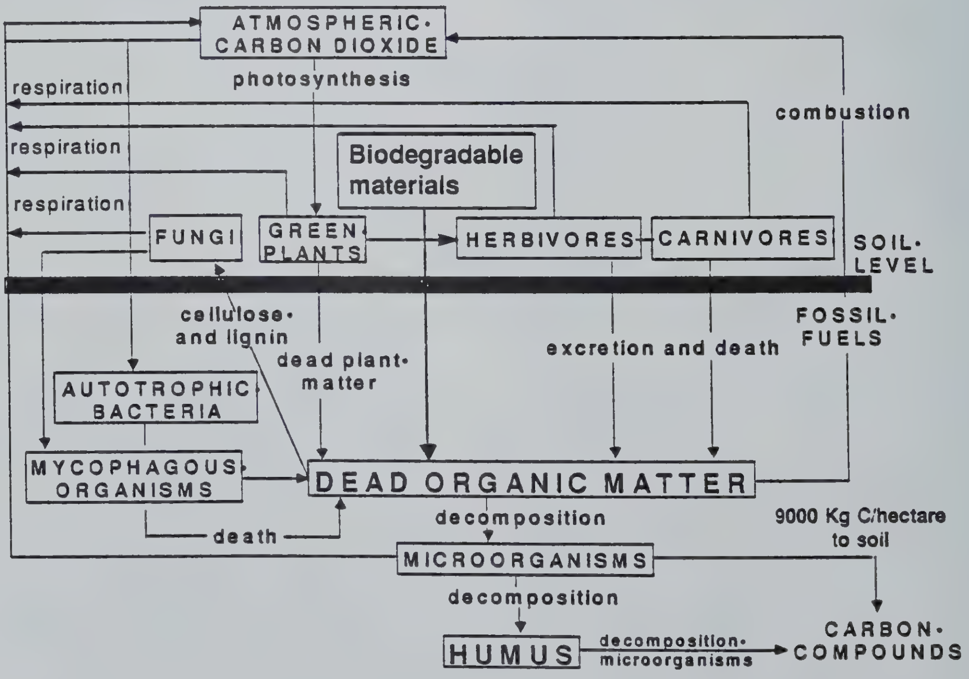

Figure 51. Biological carbon cycle.

The humic substances influence the physical properties of soil and the pathways of plant metabolism [6]. They form the living environment for the micro and macro fauna and flora to flourish.

As discussed earlier, today's polymeric materials are bioresistant. This results in an irreversible build-up of these synthetic materials in the ecosystem, thereby short-circuiting the system. Thus, the rationale is to design and engineer strong, lightweight, useful, disposable polymeric materials that break down under given environmental conditions or in appropriate waste disposal systems such that the ecosystem can assimilate the carbon by way of the carbon cycle.

4. Composting [7]

The time frames necessary for natural ecosystems to operate cannot cope with the amount of solid waste we produce and this includes both the polymeric material and the naturally degradable yard waste, paper, paperboard, etc. Furthermore, with the mix and type of solid waste generated today it would be environmentally unsound and unsafe to allow for uncontrolled and unmonitored biodegradation. Therefore, new processes that can accelerate the degradation of these wastes in a controlled manner, within the scope of the biological carbon cycle and the constraints of the ecosystem, need to be developed.

Composting is such a process and is defined as "accelerated degradation of heterogeneous organic matter by a mixed microbial population in a moist, warm, aerobic environment under controlled conditions." Polymeric materials, when designed to be biodegradable using renewable resources (agricultural products) as the major raw material component, can become part of this ecologically sound mechanism—"Nature's Recycling System." Biodegradation of such natural materials will produce valuable compost as the major product, along with water and carbon dioxide. The CO_2 produced should not contribute to an increase in greenhouse gases because it is "fixed" as part of the biological carbon cycle. Figure 52 describes the fundamental materials equation for the composting process.

By composting our biodegradable plastic and paper waste, we can generate much-needed carbon-rich soil (humic material). Compost amended soil can have beneficial effects by increasing soil organic carbon, increasing water and nutrient retention, reducing chemical inputs, and suppressing plant diseases. The problem of waste disposal could become the solution for low-input sustainable agriculture. In this sense, composting is more than just ecologically sound waste disposal, it is resource recovery.

$$C_{material} + O_2 \longrightarrow C_{CO_2} + C_{biomass/compost} + H_2O + Heat$$

$$C_{biomass\ (compost)} = C_{cellmass} + C_{humic\ material}$$

(Stabilized slow release form
of carbon , nitrogen)

↓

- no persistent/recalcitrant, synthetic, or toxic residue
- Improved soil productivity
- Supports micro and macro flora & fauna activity

Figure 52. Composting equation.

4.1 Integrating Material Design and Use With Composting Concepts

An example of such an integrated material design, use, and ultimate disposability is the program underway at Michigan Biotechnology Institute (MBI). MBI is currently developing corn based coatings for paper cups and sandwich wraps as replacement for current nonbiodegradable polyethylene and wax coatings. The new coatings have acceptable water and grease barrier properties and are compatible with both composting and paper recycling processes. Additionally, MBI is also engineering starch based moldable products that have water repellent properties, mechanical strength, good processability, and compostability, for cutlery and other applications. A demonstration program, in which these materials would be introduced into a fast-food restaurant setting, the waste collected and composted with other necessary lignocellulosic and nitrogenous wastes, is underway. The utility and value of the compost generated will be established by applying it on experimental farm land. This integrated "Cradle to Grave" material development concept is shown in figure 53.

4.2. Need for Fully Compostable Materials

The need for fully compostable materials (completely biodegradable under composting conditions) is based on composting studies on paperboard either uncoated or coated with polyethylene (plastic) or a biodegradable polymer based on corn. The studies show that the polyethylene coating was recalcitrant to biodegradation, whereas the cellulosic component (from paper) and the biodegradable polymer were completely biodegraded in the composting time frame [7]. The study documented that starting with only a few percentages of plastic

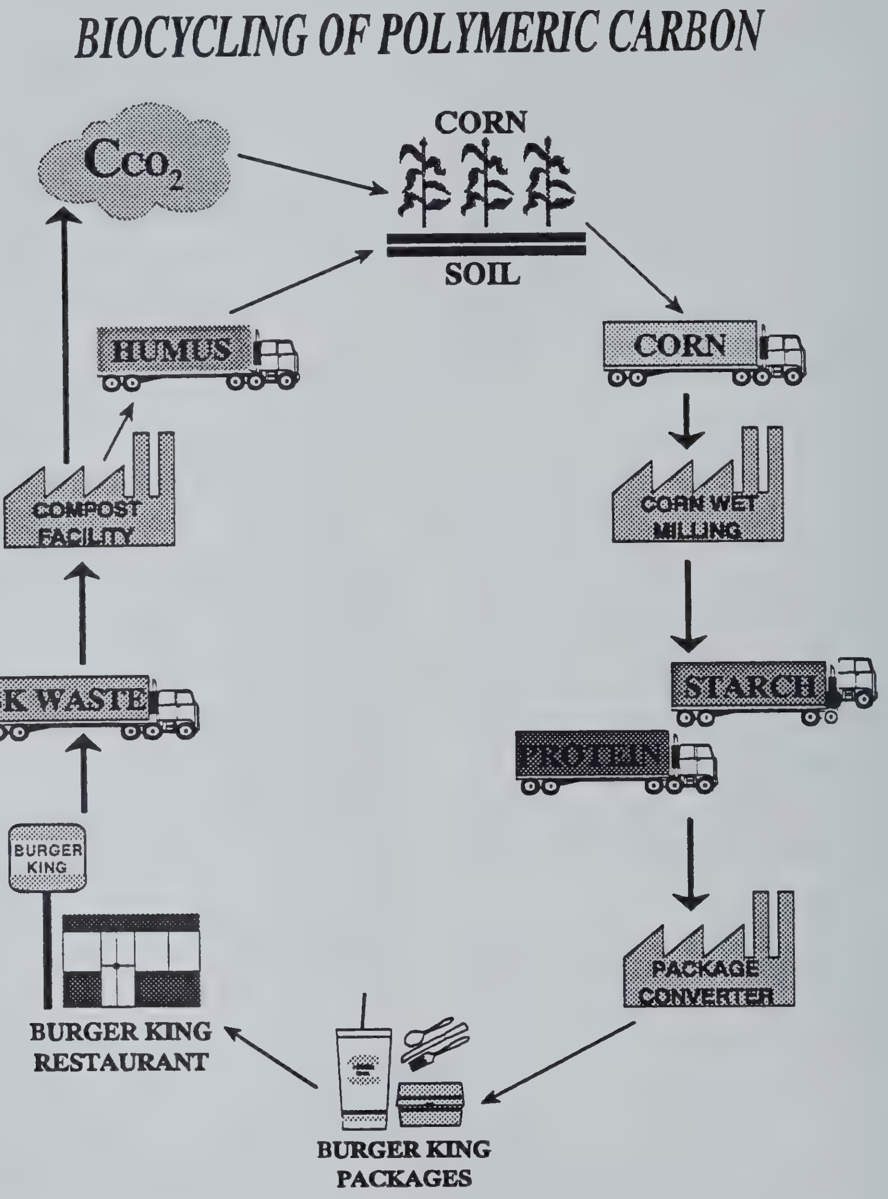

Figure 53. Cradle to grave concept for fast-food packaging and other organic wastes.

(polyethylene, PE) coating in the starting substrate, the final product contained about 50% plastic.

The paper [7] concluded that this material is not suitable for use in any type of soil application even though the PE is inert and innocuous. This is because continuous application of such material over a period of time would result in a slow build up of PE in the soil. The humic carbon would be utilized eventually. The net result would be a totally unproductive and infertile soil that would not support activities of micro and macro flora and fauna. If the ultimate goal of composting is to transform waste into usable products, then all the waste material going into a composting operation should be used and transformed leaving no persistent/recalcitrant, or toxic residues as defined in the composting equation (fig. 52) described earlier.

5. Design and Engineering of Biodegradable Plastics

As discussed earlier, polymers have been designed in the past to resist degradation. The challenge is to design polymers that have the necessary functionality during use, but destruct under the stimulus of an environmental trigger after use. The trigger could be microbially, hydrolytically or oxidatively susceptible linkages built into the backbone of the polymer, or additives that catalyze breakdown of the polymer chains in specific environments. More importantly, however, the breakdown products should be not toxic or persistent/recalcitrant in the environment and can be completely utilized by soil microorganisms. It cannot be overemphasized that, in order to ensure environmental, regulatory, and market acceptance of these biodegradable products, the ultimate biodegradability of these materials in the appropriate waste management infrastructures (like composting or sewage treatment facilities or soil) similar to the lignocellulosic materials needs to be demonstrated beyond doubt. A report [8] (Green Report II) issued by a group of State Attorney Generals states:

It may be appropriate to make claims about the "biodegradability" of a product when that product is disposed of in a waste management facility that is designed to take advantage of biodegradability and the product at issue will safely break down at a sufficiently rapid rate and with enough completeness when disposed of in that system to meet the standards set by any existent state or Federal regulations.

The U.S. Federal Trade Commission (FTC) guidelines states [9]:

> "Unqualified degradability claims should be substantiated by evidence that the product will completely break down and return to nature, that is decompose into elements found in nature within a reasonably short period of time after consumers dispose of it in the customary way . . . "

With regards to compostability claims, the FTC guidelines state:

> ". . . substantiated by evidence that all the materials in the product or package will break down into, or otherwise become part of, usable compost (e.g., soil-conditioning material in a safe or timely manner in an appropriate composting program or facility , or in a home compost pile or device. . . .")

6. U.S. Biodegradable Materials Industry

Unfortunately the U.S. biodegradable's industry fumbled at the beginning by introducing starch filled (6–15%) polyolefins as true biodegradable materials [10]. These at best were only biodisintegrable and not completely biodegradable. Data showed that only the surface starch biodegraded, leaving behind a recalcitrant polyethylene material [11, 12]. Starch entrapped within the PE matrix did not appear to be degraded.

The failure of such materials to gain widespread acceptance as an environmentally sound product was due to a number of reasons, chief among them being:

- ASTM standards for degradability and Federal Trade Commission (FTC) guidelines were not in place at that time, so companies did not have any benchmarks to target
- Lack of understanding about the rationale for biodegradable materials in the context of the environment and the ecosystem
- Unrealistic expectations driven by over selling of product capability and performance without substantiation by hard scientific data
- Opposition to change by the plastics industry

Today, biodegradable products being introduced or planned to be introduced by various companies are fully biodegradable or compostable. The need to tie in the waste management infrastructure, like composting, with use of biodegradable materials is recognized and being actively pursued. ASTM standards have been developed for determining intrinsic biodegradability, biodegradability under composting conditions, biodegradability under other environmental conditions, and environmental fate of degraded products. Many more Standards are under development. FTC guidelines on the subject of biodegradability, compostability, recyclability, and other environmental claims have been issued. Detailed scientific substantiation for the biodegradability of the new products in specific waste management infrastructures such as composting is being obtained.

Thus, in today's market place there is a much greater acceptance of biodegradable products, and a better appreciation of the role of biodegradable materials in waste management. However, the problems of the early biodegradable products, still, continues to plague the nascent biodegradable materials industry. Table 69 lists the major biodegradable materials producers and their technologies.

6.1 Polyester Based Biodegradables

Four of the technologies listed in table 69 are based on polyesters. They are:

- polylactide polymers and copolymers being commercialized by Cargill, and Ecochem (a joint venture of DuPont and Conagra)
- polyhydroxy butyrate valerate copolymers (PHBV) commercialized by Zeneca
- polycaprolactone sold by Union Carbide

Incorporation of an ester group on the backbone of the polymer opens up the polymer to attack by nonspecific esterase secreted by soil microorganisms and water (hydrolytic attack). In all probability both enzymatic and hydrolytic mechanisms operate to varying degrees during the biodegradation process. Ultimately the polymer chains are broken down into smaller molecules which are readily assimilated by soil microorganisms.

The use of polylactide polymers and copolymers for biodegradable plastics is a fertile field, and considerable R&D activity is ongoing. Argonne National Laboratories has signed a licensing agreement with a Japanese firm, Kyowa Hakko, USA for Argonne's Poly(lactic acid) technology, although commercial production is not expected for at least 2 to 3 years. The Argonne technology involves the production of lactic acid by fermentation using potato waste as the feed stock. Condensation polymerization of the lactic acid produces low molecular weight poly(lactic acid) which is then spliced together using coupling agents to give the higher molecular weights so essential for good mechanical properties. The Cargill, and Ecochem technologies involve a two-step process that converts the lactic acid to its dehydrated dimer the lactide followed by ring opening polymerization to high molecular weigh polylactide (PLA) polymers. Polylactide copolymers are prepared by copolymerization of other lactone monomers like glycolide, and caprolactone with the lactide monomer. Battelle has entered into a R&D joint venture with Golden Technologies Inc., Golden, Co. to look at PLA materials usage in commercial packaging. Polylactide polymers and copolymers are currently widely used in a number of biomedical applications like resorbable sutures, prosthetic devices, and as a vehicle for delivery of drugs and other bioactive agents.

Table 69. Major biodegradable materials producers

COMPANY	BASE POLYMER	FEEDSTOCK	COST, $/lb	CAPACITY, MM LB/YR
Cargill, Minneapolis, MN	Polylactide (PLA)	Renewable Resources, Corn	1.00 -3.00	10 ('94 scaleup); 250 (mid-1996)
Ecochem, Wilmington, DE	Polylactide copolymers	Renewable Resources, Cheese whey, corn	< 2.00 proj'd	0.15 ('94 scaleup)
Flexel, Atlanta GA	Cellophane (Regenerated cellulose	Renewable resources	2.15	100
Zeneca (business unit of ICI)	Poly(hydroxybutyrate-co-hydroxyvalerate), PHBV	Renewable resources -- carbohydrates (glucose), organic acids	8.00 - 10.00; 4.00 proj'd	0.66, additional capacity slated for '96 is 11 - 22
Novamont/Ferruzzi-Montedison, New York, NY, & Italy	Starch-synthetic polymer blend containing approx. 60% starch	Renewable resources + petrochemical	1.60 - 2.50	50, in Turni, Italy
Novon Products (Warner-Lambert Div.), Morris Plains, NJ	Thermoplastic starch polymer compounded with 5-25% additives	Renewable resources, Starch	2.00 - 3.00	100
Union Carbide, Danbury, CT	Polycaprolactone (Tone polymer)	Petrochemical	2.7	< 10
Air Products & Chemicals, Allentown, PA	Polyvinyl alcohol (PVOH) & Thermoplastic PVOH alloys (VINEX)	Petrochemical	1.0 -1.25 (PVOH); 2.50-3.00 (VINEX)	150 - 200 (water sol. PVOH); 5 (VINEX)
National Starch & Chemical, Bridgewater, NJ	Low ds starch ester	Renewable resources, Starch	2.00 - 3.00	Not available
Planet Packaging Technologies, San Diego, CA	Polyethylene oxide blends (Enviroplastic)	Petrochemical	3	10
Showa Highpolymer Co., Ltd.	condensation polymer of glycols with aliphatic dicarboxylic acids (BIONELLE)	Petrochemical	approx. 3.00; 800 yen per Kg	0.2 (pilot); 7(semi-commercial, end '94)

Poly(hydroxybutyrate) (PHB), and poly(hydroxybutyrate-co-hydroxyvalerate) (PHBV) are novel thermoplastic polyesters that are prepared by a bacterial fermentation process using a variety of feed stocks including glucose and acetic acid. PHB is a brittle polymer. However, the introduction of hydroxyvalerate groups in the polymer backbone (0–30%) reduces the crystallinity, and the resultant material is much more ductile and flexible. A good balance of properties can be achieved by varying the comonomer content to yield polymers for specific applications. PHBV is currently in commercial use for blow molded shampoo bottles in the United States, Japan, and Germany. It is also being used to make razor handles in Japan. There is a considerable body of literature in this field and the reader is referred to papers by Holmes [13, 14] and Galvin [15] and the references cited in them. There is considerable R&D activity in the field of bacterial polyesters under the general name of polyhydroxyalkanoates and the subject of yearly International Symposia [16].

Poly(e-caprolactone) (PCL) is sold under the trade name of Tone polymers by Union Carbide. Grades of PCL have been commercially available since 1975 and used in coatings and in elastomers. More recently film extrusion of PCL resins have been reported [17]. Blends of PCL with linear low-density polyethylene (LLDPE) have excellent film forming capabilities, however the issue of biodegradability of the PE segment still remains. Clendinning et al. [18] describe degradable transplanter containers that are a blend of PCL and PE containing a polyvalent transition metal salt with a auto-oxidizable additive. The container disintegrated in soil, but the degradability of the PE component was not addressed.

6.2 Natural Polymer Based Biodegradables

Naturally occurring biopolymers like starch and cellulose are readily biodegradable. As shown in table 1, two companies (Novon, and Novamont) are commercializing starch based thermoplastic technologies. Basically, these technologies involve thermoplasticization of the starch using water and heat under pressure. The starch is heated above the glass transition and melting temperature of its components. This results in disruption of the molecular structure resulting in a "destructurized starch" that has thermoplastic properties. A number of polymer compositions containing destructurized starch for different applications has been described [19].

Cellulose is readily biodegradable, and regenerated cellulose film made by the viscose process still finds many applications [20]. Table 69 lists one of the cellophane producers. DuPont, one of the major suppliers of cellophane, is no longer making it as a result of poor economics and competition with other olefin polymers. Furthermore, the viscose process of making cellophane has negative environmental impacts. Because cellophane is inherently biodegradable, it has much promise for film applications and could potentially capture some of the markets it lost to the non-degradable olefin polymers. However, an economical, more environmentally benign process for manufacture would have to be engineered. Cellulose esters like cellulose acetate, and mixed esters like cellulose acetate butyrate are commercial products on the market. However, the high degree of substitution of the ester groups (2.4 out of a maximum of 3) renders these plastics nonbiodegradable.

6.3 Other Degradable Plastics

As shown in table 69, poly(vinyl alcohol) (PVOH) is a readily biodegradable water soluble polymer. However, this polymer cannot be processed by conventional extrusion technologies. This is because the melting point of PVOH is around 23O °C for the fully hydrolyzed grade and around 180–190 °C for the partially hydrolyzed grade. However PVOH undergoes rapid decomposition above 200 °C Therefore these films can only be prepared by solvent casting from water. Recently, Air Products has come up with a modified PVOH resin that retains its water solubility but is extrudable. This has been achieved by incorporating a internal plasticizer by hydroxyethylation of the -OH group (reaction with ethylene oxide), solvolysis of a graft copolymer of vinyl acetate onto polyalkyelene glycols. Air Products introduced the thermoplastic, water soluble resins under the trade name of VINEX. Vinex is a copolymer of PVA with poly(alkyleneoxy) acrylate.

Photodegradable plastics are produced by incorporation of photosensitive groups or additives into the plastics. Exposure to sunlight (UV radiation) causes radical induced polymer degradation. The main goal in the design of photodegradable plastics is to cause accelerated embrittlement of the plastics on exposure to sunlight as a way of addressing litter and hazards posed to marine life. Federal law requires six-pack ring connectors to be degradable because of the choking hazard posed by these connectors to marine life due to the littering of these ring connectors on beaches. Photodegradable plastics have also found applications as agricultural mulch films. The ethylene-carbon monoxide (E-CO) copolymer is commercially used by ITW, Illinois, to make photodegradable six-pack ring connectors. While these plastics embrittle on exposure to sunlight, the biodegradability of the resultant breakdown products is questionable. Other photo triggers used are vinyl ketone copolymers in place of CO and transition metal catalyst additives [see papers by J. E. Guillet, G. Scott, D. Gilead, L. K. Ballinger, and F. C. Schwab in Ref. [8].

7. Markets

The major target markets for biodegradable polymeric materials are:

- single-use, disposable packaging materials
- Consumer goods—items like cups, plates, cutlery, containers, egg cartons, combs, razor handles, toys etc.
- disposable nonwovens (diapers, personal care and feminine hygiene products, certain medical plastics)
- coatings for paper and film

More than 50 billion pounds of paper and plastic are disposed of annually in these markets. In food packaging, it's around 19 billion pounds, in nonfood packaging, it's 17 billion pounds, in personal and healthcare, 7 billion pounds, and other disposables 7 billion pounds. Compared to the potential market volume, the announced capacity of the existing biodegradable plastics producers (table 69) is minuscule. While biodegradable materials are not expected to completely replace all of the plastics currently used in these markets, they represent a exciting, huge business opportunity waiting to be seized. The potentially "compostable components" in the plastics and paper segments of the municipal solid waste stream representing market opportunities for biodegradable plastics is shown in figure 50 (also refer to earlier discussion on fig. 50 in Sec. 2).

7.1 Packaging and Consumer Goods

In 1989, 14.7 billion pounds of synthetic resin were used for packaging in the United States. That figure represented 28% of the total resin used in 1989, making packaging the leading category over such segments as building and construction, and consumer and institutional products [21]. It is projected that by the year 2002, this number would increase to 24.5 billion pounds. Table 70 lists volume of plastic used in packaging by resin type and processing mode for 1992 [22] and amounts to 9.3 billion pounds. These resins are potential candidates for replacement by biodegradable plastics.

Food packaging and especially fast-food packaging is being targeted for composting because of the large volume of paper and other organic matter in the waste stream. Thus, these plastic markets would require biodegradable plastics that are compatible with the up and coming waste management infrastructure of composting. Figure 54 shows the composition of fast-food restaurant waste. It can be seen that the major component of the waste stream is readily compostable "organic waste" with a small percentage of nonbiodegradable plastics. Thus, replacing the nondegradable plastics with biodegradable plastics will render this waste stream fully compostable and help convert waste to useful soil amendment. The interesting statistic shown in figure 54 is that 70% of customer orders are drive-thru take-out orders. As home composting grows, the demand for biodegradable plastics in these markets will increase.

Table 71 lists some specific, single use, disposable polystyrene market segments where the products do not lend themselves to recycling and are excellent, immediate targets for replacement by biodegradable plastics. Novon and National Starch & Chemical are already marketing starch based loose-fill packaging that is water soluble and biodegradable yet have the resilience and compressibility of polystyrene.

7.2 Nonpackaging Markets

Markets for biodegradable plastics are not restricted to packaging alone. Table 72 shows polyethylene based nonpackaging film applications amounting to 2.6 billion pounds that can potentially be captured by biodegradable plastics. In agricultural applications like mulch film, 221 MM lb. of low-density polyethylene film was used in 1991. A biodegradable agricultural mulch film would represent an energy and cost saving to the farmer because he would not have to retrieve the nondegradable film from the field. In such cases biodegradability is both a functional requirement and an environmental attribute.

The area of disposable nonwovens like diapers, personal and feminine hygiene products and certain medical plastics like face masks, gowns, gloves, etc., are excellent candidates for replacement with biodegradable plastics. This is a growing market segment and these products do not lend themselves to recycling concepts.

Table 70. Potential packaging markets for biodegradable plastics

Application & Material type	MM lb
HD Polyethylene	
Blow molded containers	2,525
Injection molded	1,099
Closures	81
Film	682
TOTAL	**4,387**
LD Polyethylene	
Blow Molded	82
Injection molded	230
Film	3,740
Closures	33
TOTAL	**4,085**
Polypropylene	
Blow molded	137
Extruded	52
Injection molded	208
Thermoformed	58
Closures	426
Oriented film	512
Unoriented film	142
TOTAL	**1,535**
Polystyrene	
Blow molded	9
Molded -- solid	162
Molded -- foam	90
Thermoformed --foam	475
Thermoformed -- impact	440
Thermoformed --oriented sheet	30
Closures	201
Film	210
TOTAL	**1,617**
Polyvinyl chloride	
Blow molded	195
Thermoformed	161
Closures	75
Film	240
TOTAL	**671**
Polyethyleneterephthalate (PET)	
Blow molded	1,200
Thermoformed	160
TOTAL	**1,360**
GRAND TOTAL	**9,268**

Table 71. Specific polystyrene markets that are excellent candidates for biodegradable materials

MARKET	MM lb
Polystyrene Based	
Molded articles	
Produce baskets	22
Tumblers & Glasses	80
Flatware, cutlery	90
Dishes, cups and bowls	55
Extrusion (solid) articles	
Dairy containers	142
Vending & portion cups	255
Lids	110
Plates & bowls	40
Extrusion (foam)	
Stock food trays	185
Egg cartons	55
Single-service plates	135
Hinged containers	100
Cups (non-thermoformed)	40
Expandable bead	
Packaging	101
Cups and containers	148
Loose fill	75
TOTAL	1,633

Table 72. Nonpackaging film markets for biodegradable plastics

MARKET	MM lb
Agriculture	221
Diaper backing	235
Household	181
Industrial sheeting	238
Non-woven disposables	53
Trash bags	1,322
Miscellanous	336
TOTAL	2,586

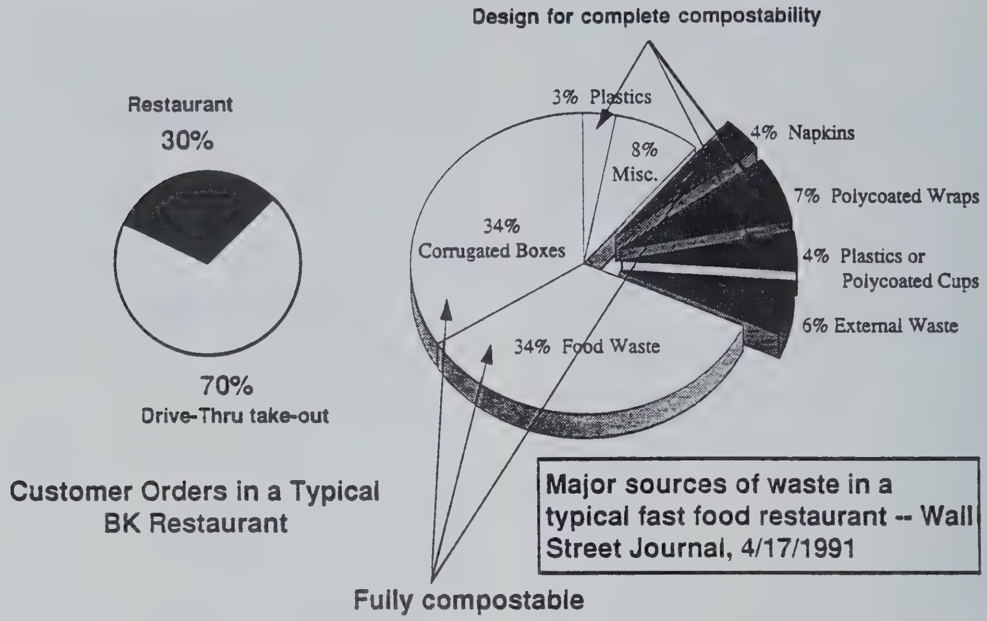

Figure 54. Composition of fast-food restaurant waste.

Table 73. Potential coatings markets for biodegradable materials

Coatings Resin	MM lb
Epoxy	36
EVA copolymer	75
Polyethylene, HD	81
Polyethylene, LD	815
Polypropylene	20
Polyvinyl acetate	48
Polyethylene terepthalate(PET)	12
Polyvinyl chloride	23
Other	96
TOTAL	1,206

Table 73 lists the resins used in coatings for packaging. As discussed earlier, coatings for paper and paperboard are excellent markets for biodegradable materials. Paper recycling and soiled paper and paperboard composting are already taking place and will grow in the years to come. A compostable/biodegradable paper coating that does not interfere in the recycling operations is needed and is being eagerly sought by manufacturers of paper products world-wide.

8. Business Opportunities

There are two major areas for small businesses to get into. The first obvious one is to design and engineer fully biodegradable plastics that have the required functional requirements for the markets discussed earlier. The other very profitable and promising area for existing and new small businesses is in the down-stream processing of biodegradable resins currently being produced (table 69).

8.1 Design and Engineering of Fully Biodegradable Plastics

Natural polymers are inherently biodegradable and, therefore, are excellent candidates as starting materials for biodegradable plastics. However, these polymers will have to be converted into a thermoplastic material by physical or chemical modification or both. In this chapter, biodegradable plastics based on natural polymers like starch and cellulose have been discussed, however, there are many more that can be exploited either by themselves or in combination with starch and cellulose. Examples of natural polymers that have promise are chitin, levan, pullulan, and protein polymers. As has been done in the case of starch, physical modification and the use of plasticizers can potentially transform these polymers into readily processable, thermoplastic materials. Chemical modification of natural polymers can potentially convert them into thermoplastic materials like the cellulose esters. However, care must be taken to ensure that the chemically modified polymer still retains its biodegradability, for example cellulose is readily biodegradable, cellulose triacetate and cellulose acetate (degree of substitution of 2.4) are not biodegradable.

The search for biodegradable plastics need not be restricted to natural polymers. Aliphatic polyesters (for example, polycaprolactone—see Sec. 6.1) and other synthetic polymers which have been discarded because of its degradability can potentially be engineered to provide function utility for a specific time period and ultimately biodegrade.

8.2 Compounding and Processing of Biodegradable Resins

There are a number of small business extrusion and molding companies throughout the U.S. that could tie in with the major biodegradable resin producers (table 69) and work with them in compounding and fine-tuning the processing of these new resins for specific product applications. Injection molding, for example, is a major processing technique for converting thermoplastic materials and accounts for almost 20% of U.S. resin production. Small businesses that are in the sheet, cast, and blown film markets or new business entrepreneurs could exploit the emerging biodegradable materials for new business opportunities.

Modification through filler and fiber reinforcement, additive compounding, and formulation engineering would be needed to move the biodegradable plastics into the market place. Compounders are needed to formulate application specific materials through blending and alloying, filling and fiber reinforcement, or other specialty modifications.

Biodegradable plastics offers a new business opportunity with good growth potential for the enterprising small business plastic processor. Environmental and societal concerns is driving the change towards new materials that require ultimate disposability built into the materials — Biodegradable and Recyclable materials. In order to remain successful in a very competitive field the small business plastic processor must adapt to meet the processing requirements of these new materials.

9. Degradable Plastics Standards

ASTM, a voluntary, not-for-profit Standards organization created a subcommittee under its Technical Committee on Plastics (D-20) to address the issue of standards for degradable plastics. The scope of the subcommittee was "The promotion of knowledge, and the development of standards (Classification, guide, practice, test method, terminology, and specification) for plastics which are intended to environmentally degrade. Currently, there are 170 plus members on the subcommittee and they represent a broad spectrum of interests ranging from producers, users, consumers, and general interest. Industry, government, academia, and National laboratories all have representatives on the subcommittee. One does not have to be a regular paying member of ASTM to participate in the standards development activities of the subcommittee. The subcommittee is further divided in to sections to address various aspects of degradability. The sections under D-20.96 are:

- Biodegradable (D-20.96.01)
- Photodegradable (D-20.96.02)
- Chemically degradable (D-20.96.03)—hydrolytic, & oxidative
- Environmental Fate (D-20.96.04)
- Terminology (D-20.96.05)
- Classification & Marking (D-20.96.06)

9.1 Photodegradable Standards

Two Standard Practices for exposure of photodegradable plastics to simulated test environments have gone through the "ASTM consensus process" and published as a ASTM Standard. The two are:

- Standard Practice for operating Xenon Arc Type exposure apparatus with water for exposure of photodegradable plastics (D5071-91)
- Standard Practice for operating fluorescent UV and condensation apparatus for exposure of photodegradable plastics (D5208-91)

A Standard Practice for determining degradation end-point in degradable polyolefins using a tensile test has been published as a society standard (D3826-91). This practice determines the degradation end point (brittle point) for degradable polyethylene and polypropylene films and thin sheeting. The standard establishes loss in structural integrity of the degraded plastic material and is a valuable end-point for degradable plastics designed for litter control, and mitigating strangulation hazards posed to marine life. This method would apply to biodegradable plastics and establish loss in structural integrity, i.e., biodisintegration. A round-robin inter-laboratory study is being initiated to determine Precision and Bias for this test method.

Another Standard Practice for Outdoor Exposure Testing of Photodegradable Plastics has also cleared and is ready to be published as a ASTM standard. Two practices for establishing degradability of polystyrene using dilute-solution viscosity and tumbling friability are at main committee ballot and should soon become an established standard.

9.2. Biodegradable Standards

Test methods to measure the intrinsic biodegradability of plastic materials designed for biodegradability have cleared society balloting and are full-fledged ASTM standards. The test method measures the percent conversion of the carbon from the designed biodegradable plastic to CO_2 in a aerobic environment and CH_4 (plus some CO_2) in a anaerobic environment. The test material is the sole carbon source for the microorganism in the experiment. The two bio-test methods are:

- Standard Test Method for Determining the Aerobic Biodegradation of Plastic Materials in the Presence of Municipal Sewer Sludge (D5209-91)
- Standard Test Method for Determining the Anaerobic Biodegradation of Plastic Materials in the Presence of Municipal Sewer Sludge (D5210-91)

Three other bio-test methods have become ASTM Standards. They are:

- Standard test method for assessing the aerobic biodegradation of plastic materials in an activated sludge-waste water treatment system (D5271-92)
- Standard test method for determining the aerobic biodegradation of plastic materials under controlled composting conditions (D5338-93)
- Standard test method for determining the aerobic biodegradability of degradable plastics by specific microorganisms (D5247-92)

The first two simulate environments that are representative of waste management infrastructures such as composting and waste-water treatment system. The test methods permit one to quantify biodegradability in specific waste management infrastructures. While these test methods give a quantitative measure of biodegradability in such environments, parallel tests in "real world systems" need to be run to confirm and establish biodegradability. ASTM is currently developing standard practices for exposing degradable plastics to such "real systems" environments and reporting the reasultant data. The specific microorganisms test method does not represent any real world waste management infrastructure but provides a standard test method to quantify biodegradability using well-defined microbial cultures commonly present in the environment.

Aquatic Biodegradability: Mitigating the hazards to marine life by designing bio and photodegradable plastics that would degrade in a marine environment is one of the targets for industry. Thus, to evaluate the biodegradability potential in an aquatic environment, Standard Practices for Exposing Plastics to a Simulated Marine and Fresh-Water Environments were developed and are now at the Society balloting stage. A Standard Test Method to quantify the amount of degradation in such environments is currently being developed and will build on the two aquatic test practices discussed.

Composting Environment: Composting is fast becoming a important waste management strategy. Biodegradable plastics that will be compostable in an appropriate composting infrastructure are being designed. As discussed earlier, a Standard Test Method for Determining the Aerobic Biodegradation of Plastic Materials under Controlled Composting Conditions has been developed. A Test Practice for Exposing Plastics to a "Real World" Simulated Compost Environment is under development.

Soil Environment: Test Practices and Methods for determining the biodegradability potential in soil burial tests are under development.

Others: A number of other specific test methods are under various stages of development for example, a high solids anaerobic digestor system, accelerated (biologically active) landfill conditions.

9.3 Fate and Effects Testing on Biodegraded Products

One of the major issues raised in connection with degradable plastics is the fate and toxicity of the degraded products. A Standard Practice for Water Extraction of Residual Solids from Degraded Plastics for Toxicity Testing has been developed. It is a published ASTM Standard (D 5152-91) having successfully going through the ASTM consensus process. The practice is essentially a "bridging" practice to prepare samples from degraded plastics for aquatic toxicity testing using established toxicity test methods such as ASTM methods D 4229, E 1192, E 1295 or other currently accepted toxicity test methods. A round-robin inter-laboratory testing to demonstrate the utility of the existing practice is being initiated. A similar "bridging" practice for preparing degraded plastic samples for terrestrial toxicity testing is under development. In the area of composting this would extend to establishing that the compost can promote microbial and plant growth, and leave behind no persistent/recalcitrant or toxic residue.

9.4 Marking and Classification

The purpose of developing a marking scheme for degradable plastics is to identify the plastic as a degradable plastic and delineate its type, i.e., photo, bio, oxidative, hydrolytic. Having such markings would promote the disposal of such plastics in appropriate waste management infrastructures such as composting or sewage treatment plants. It would also ensure that these plastics do not end up in other segregated waste streams. The marking does not certify the degradability of the plastic for which appropriate Standard Test Methods must be employed.

It is envisioned that as data are accumulated on degradable plastics using the ASTM Test Methods a classification scheme would evolve. Conceptually this would be based on the time period to achieve a specific degradation end-point.

9.5 Terminology and Definitions

ISO 472:1988 (International Standards Organization).

Degradation — A change in the chemical structure of a plastic involving a deleterious change in properties.

Deterioration — A permanent change in the physical properties of a plastic evidenced by impairment of these properties.

ASTM D-20.96 Definitions

Degradable plastic — A plastic designed to undergo a significant change in its chemical structure under specific environmental conditions resulting in a loss of some properties that may vary as measured by standard test methods appropriate to the plastic and the application in a period of time that determines its classification.

Biodegradable plastic — A degradable plastic in which the degradation results from the action of naturally-occurring micro-organisms such as bacteria, fungi and algae.

Photodegradable plastic — A degradable plastic in which the degradation results from the action of natural daylight.

Oxidatively degradable plastic — A degradable plastic in which the degradation results from oxidation.

Hydrolytically degradable plastic — A degradable plastic in which the degradation results from hydrolysis.

10. Conclusions

A growing environmental awareness on the need to address the ultimate disposability of materials has generated considerable interest in recyclable and biodegradable plastic materials. A nascent biodegradable plastics industry has evolved. The rationale is to make certain single use, disposable packaging and consumer goods biodegradable, and compost them along with other organic waste to soil humic materials. The emphasis being placed on composting as an ecologically sound waste management technique opens up markets for biodegradable plastics especially in the food packaging, personal and health care products, certain consumer goods, and some non-packaging applications. The market volumes are huge, totaling around 20 billion pounds annually. Current and projected biodegradable resin capacity targets only a fraction of this huge market. This is a tremendous market opportunity for small business to design new biodegradable materials for specific markets. Another business opportunity for small business is in the area of downstream compounding and processing of existing biodegradable resins.

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Near Term Application of Biotechnology to Fuel Ethanol Production from Lignocellulosic Biomass

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Substantial improvements over the last 10 years in enzyme-based conversion technologies for production of ethanol from lignocellulosic biomass now make commercial entry potentially attractive. In particular, opportunities are emerging to produce ethanol from low-cost sources of lignocellulosic biomass such as agricultural and forestry residues, municipal solid waste, and industrial wastes at costs less than the current price of ethanol from corn. A dilute acid pretreatment step results in high yields of fermentable sugars from the hemicellulose fractions of biomass as well as opening up the biomass structure to facilitate conversion of the cellulose into glucose. The simultaneous saccharification and fermentation (SSF) process breaks down the major cellulose fraction to glucose sugar and rapidly ferments glucose to ethanol. Through application of modern genetic engineering and other approaches, several technologies have emerged that provide high yields of ethanol from the previously difficult to utilize hemicellulosic sugars. Developments in these and other areas have reduced the projected selling price of ethanol from about $0.98/liter ($3.70/gallon) 10 years ago to only about $0.32/liter ($1.23/gallon) now for feedstocks costing $46/dry tonne ($42/ton). When niche opportunities such as use of inexpensive sources of lignocellulosic biomass or inexpensive debt financing are available, the projected costs can drop sufficiently below the approximate $0.35/liter ($1.32/gallon) selling price of ethanol made from corn to provide promising venture opportunities. The implementation of the Clean Air Act Amendments of 1990 provides ethanol with an immediate market as an oxygenate for blending with gasoline to reduce emissions of carbon monoxide and unburned hydrocarbons from vehicle exhaust. Addition of ethanol to gasoline also increases octane while reducing gasoline consumption. Some uncertainty has developed about the market for ethanol for direct blending with gasoline because of concern about increased evaporative losses of hydrocarbons and the potential impact of these components on ozone formation. Commercial processes are being introduced to react ethanol with isobutylene to form ethyl tertiary butyl ether (ETBE) that enjoys the same benefits as direct ethanol blends while reducing evaporative emissions from the gasoline blend. In the longer term, opportunities have been identified to reduce the price of ethanol to be competitive with gasoline without tax incentives. Large-scale substitution of ethanol derived from lignocellulosic biomass offers improved urban air quality, no net contribution of carbon dioxide to the atmosphere, improved international competitiveness, new markets for agricultural products, and substantial reductions in petroleum imports from unreliable sources.

Key words: biomass; economics; enzymatic conversion; ethanol; lignocellulosic.

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1. Introduction

Ethanol, a liquid fuel produced by fermenting sugars from biomass or by the catalytic hydration of ethylene, is an excellent transportation fuel. In recent years, interest in ethanol as an octane enhancer and fuel extender has increased dramatically in response to concerns associated with conventional transportation fuels. The implementation of the Clean Air Act Amendments of 1990 presents a potentially large and expanding market for ethanol as an oxygenate to improve air quality.

With OPEC controlling 75% of the world's oil reserves and approximately 50% of all petroleum used in the United States being imported, our nation is extremely vulnerable to oil supply interruptions. The Office of Technology Assessment projects that the United States will import about 61% of its petroleum by 2010 (U.S. Congress 1990). Petroleum imports can account for about 40% of the U.S. balance-of-payments deficit (Lynd et al. 1991a). Air quality problems such as ozone formation and carbon monoxide pollution result from use of gasoline in automobiles in many cities (U.S. EPA 1989). In addition, some predict that global climate change will result from carbon dioxide accumulation caused by burning petroleum and other fossil fuels (Intergovernment Panel on Climate Changes 1990). More and more agricultural land is being idled as crop productivity increases, resulting in a loss of agricultural income and employment (U.S. Department of Agriculture 1987). Eventual large-scale substitution of ethanol produced from renewable resources can improve energy security, reduce the balance-of-payments deficit, decrease urban air pollution, reduce accumulation of carbon dioxide in the atmosphere, and revitalize the farm economy (Lynd et al. 1991a).

Production of ethanol from sugar and starch has been practiced commercially for a number of years; however, large scale production of ethanol from these resources could increase its cost considerably. Although ethanol is made from ethylene for chemical applications, this technology has been displaced by fermentation ethanol for fuel use. Ethanol can also be made from lignocellulosic biomass, an inexpensive feedstock potentially available in large quantities. Acids or enzymes can break down the cellulose and hemicellulose chains that comprise the major fraction of the lignocellulose into their component sugar molecules for fermentation into ethanol. The challenge is to develop low-cost methods to convert the naturally resistant cellulose and hemicellulose economically. Through research advances achieved over the last few years, this technology has reached the point of commercial promise for use as a gasoline additive, and production of ethanol from low-cost renewable sources of lignocellulosic biomass such as agricultural and forestry residues and a significant fraction of municipal solid waste (MSW) provides immediate opportunities for profitable business ventures.

This chapter will focus on the production of ethanol from lignocellulosic biomass by fermentation and the comparison with existing technology for ethanol production from starch. First, an overview is provided of the use of ethanol as a blending agent and a neat fuel. Then a discussion is provided of the technology and economics for ethanol production from corn and lignocellulosic biomass. Energy balance considerations and implications for carbon dioxide accumulation are covered as well for ethanol from lignocellulosic biomass. The remaining sections of the chapter are organized in business plan format. In this vein, the strengths, weaknesses/barriers, opportunities, and threats/competition are discussed for ethanol production from biomass. Then the economic basis for development of a new business based on ethanol production from biomass is summarized. The intent is to facilitate adaptation of this information to the development of new profitable businesses based on immediate opportunities for commercialization of ethanol-from-biomass conversion technology.

2. Ethanol Fuel Properties and Value

Ethanol is currently added to gasoline in the United States to form a blend of 10% ethanol with 90% gasoline (called gasohol in the past). In Brazil, ethanol is also used as a hydrous ("neat") fuel; i.e., a fuel of about 95% ethanol and 5% water, as well as blended with gasoline. Table 74 summarizes the properties of ethanol compared to selected other fuel additives, gasoline, and methanol (Wyman and Hinman 1990).

2.1 Direct Ethanol Blends

When blended with gasoline, ethanol provides several benefits. First, it can be viewed as a fuel extender that replaces a portion of the gasoline with ethanol. In this case, the ethanol value is equal to the cost of the gasoline mixture that it displaces. Because ethanol has a lower heating

Table 74. Fuel properties for ethanol, methanol, ETBE, MTBE, isooctane, and gasoline

Property	Ethanol	Methanol	ETBE	MTBE	Isooctane	Unleaded Regular Gasoline
Formula	C_2H_5OH	CH_3OH	$(CH_3)_3COC_2H_5$	$(CH_3)_3COCH_3$	C_8H_{18}	C_4 TO C_{12}
Molecular Weight	46.07	32.04	102.18	88.15	114	NA[3]
Density, kg/m³ @ 298 K	790	790	750	740	690	720-780
Air/Fuel Stoichiometric Ratio						
Mole Basis	14.29	7.14	42.86	35.71	59.5	57.28
Mass Basis	9.02	6.48	12.10	11.69	15.1	14.6
Higher Heating Value, kJ/kg	26,780	19,919	36,031	35,270	44,420	41,800-44,000
Lower Heating Value, kJ/L	21,156	15,736	27,023	26,100	30,650	31,350-33,000
Research Octane Number (RON)	106	106	118	106	100	91-93
Motor Octane Number (MON)	89	92	102	99	100	82-84
(RON + MON)/2	98	99	110	103	100	88
Blending RON	114-141[1]	135	117-120[2]	118	NA[3]	NA[3]
Blending MON	86-97[1]	105	101-104[2]	101	NA[3]	NA[3]
(BLENDING RON+MON)/2	115	120	111	110	NA[3]	NA[3]
Atmospheric Boiling Pt., K	351.6	337.8	344.8	328.6	398	300-498
Heat of Vaporization, kJ/kg	839	1104	308	329	406	377-502
Flash Pt., K	285	280	253	245	261	<233
Ignition Pt., K	697	737	583	733	683	553-702
Reid Vapor Pressure, kPa						
Pure Component	15.85		30.3	53.8		48.3 + 96.5
Blending	82.7-186	214+	20.7-34.5	55.1		55.1-103.4
Water Solubility, weight %						
Fuel in water	100	100	2	4.3	negligible	negligible
Water in fuel	100	100	0.6	1.4	negligible	negligible
Water Azeotrope, (atm b.p.), K	351.4	NA[3]	338.2	325.4	NA[3]	NA[3]
Water in Azeotrope, wt %	4.4	NA[3]	4.0	3.2	NA[3]	NA[3]

[1] 10% blends
[2] Assumed 12.7% blend
[3] Not Applicable
Source: Piel 1992; Ing. 1976; Exxon 1988; Bailey and Russell 1980; Pearson 1993.

value of about 21 megajoules/liter (76,000 Btu/gallon), while gasoline has a lower heating value of about 32 megajoules/liter (115,000 Btu/gallons), the value of ethanol as a fuel extender, V_e, is equal to the ratio of the lower heating value of ethanol, LHV_e, divided by the lower heating value of gasoline, LHV_g, times the price of gasoline, P_g:

$$V_e = (LHV_e/LHV_g)\ P_g.$$

Accordingly, ethanol would be worth about 66% as much as gasoline. As shown in figure 55, if gasoline sells for about $0.16 to $0.17/liter ($0.60 to $0.64/gallon) at the refinery gate, ethanol would only be worth about $0.11/liter ($0.42/gallon), well below the current wholesale price of ethanol.

Studies by Southwest Research Institute (Tosh et al. 1985) as well as others have shown that there is no statistically significant difference in mileage traveled on a given volume of fuel for vehicles operated on ethanol blends compared to those operated on straight gasoline. This result implies that ethanol, when blended with gasoline, provides the same range and therefore, effective energy content, as gasoline. Thus, the value of ethanol would be equal to the price of the gasoline it replaces or about $0.16 to $0.17/liter ($0.60 to $0.64/gallon). This is still far lower than the current selling price of ethanol. However, the U.S. government currently provides a tax incentive equal to $0.14/liter ($0.54/gallon) of ethanol from renewable resources (e.g., corn or lignocellulosic biomass), thereby increasing its value accordingly, and a blender is willing to pay about $0.30/liter ($1.15/gallon) for ethanol just as a replacement for gasoline (fig. 55). This tax incentive is scheduled to expire in the year 2000.

Ethanol has a blending octane of 115, and when ethanol is blended with gasoline, it increases the octane of the fuel mixture compared to the gasoline from which it is made. As a result, ethanol increases the value of the mixed fuel compared to the blending stock to which it is added, and the price that a blending company is willing to pay for ethanol as a octane booster is given by the following relationship:

$$(P+\Delta p)f+P(1-f)=P+V$$

in which P is the price of the base gasoline in which ethanol is added, Δp is the additional price that the blender is willing to pay for ethanol, V is the increase in value of the blended fuel, and f is the fraction of ethanol added to gasoline. This relationship is on a volumetric basis and neglects the small changes in volume when gasoline and ethanol

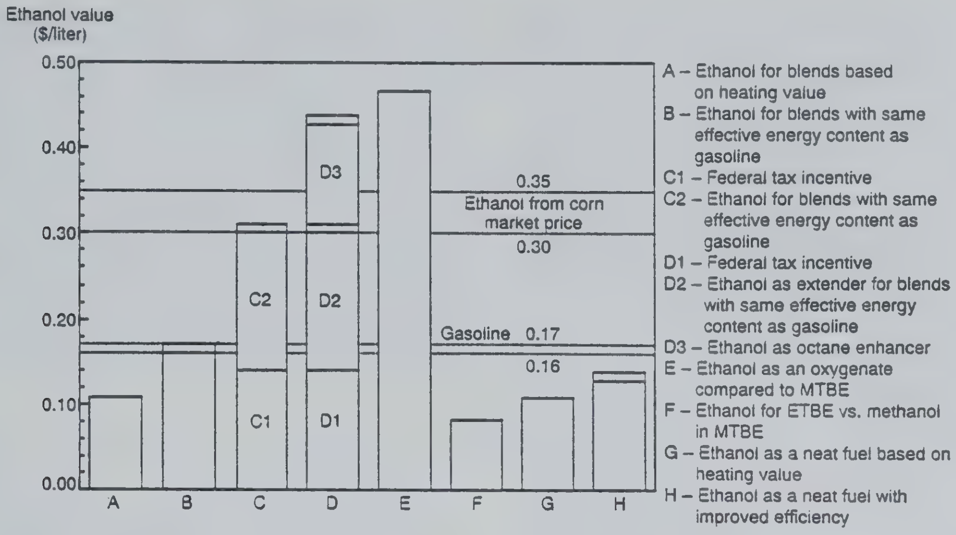


Fig. 55. The value of ethanol as a direct blending agent, for production of ETBE, and for use as a neat fuel.

are blended together. From this equation, an expression can be derived for the additional price Δp that the blender is willing to pay for ethanol:

$$\Delta p = \frac{V}{f}.$$

When ethanol is blended with gasoline to form a 10% mixture, the octane level of the gasoline is increased from regular to above that of mid-grade. If mid-grade is worth 1.3 cents/liter (5.0 cents/gallon) more than regular gasoline, ethanol will be worth $0.13/liter ($0.49/gallon) more than the gasoline to which it is added. Thus, if we assume our base gasoline price is $0.16 to $0.17 liter ($0.60 to $0.64/gallon), the total price that the blender would be willing to pay for ethanol now becomes on the order of $0.30/liter ($1.15/gallon). When the federal tax incentive of about $0.14/liter ($0.54/gallon) is added, the blender can afford to pay $0.44/liter ($1.66/gallon) for ethanol as shown in figure 55. This is well above the current market price of about $.30 to $0.35/liter ($1.15 to $1.35/gallon). An additional advantage is the ability to displace aromatics.

In addition to increasing the octane of the fuel to which it is blended, ethanol provides oxygen in the blended gasoline. The addition of oxygen to gasoline is now mandated during the winter months for carbon monoxide non-attainment areas under the Clean Air Act Amendments of 1990. Addition of oxygen will also be required for reformulated gasoline in ozone non-attainment areas beginning in 1995. Thus, it is necessary for blenders to find inexpensive sources of oxygen to use in gasoline. At the current time, the primary oxygenates used are ethanol and methyl tertiary butyl ether (MTBE). Ignoring other factors impacting what a blender is willing to pay for ethanol, the value of ethanol, V_e, as an oxygenate is given by the following relationship in terms of the price of competing products on a volumetric basis:

$$V_e = \frac{n_e\, \rho_e\, M_o}{n_o\, \rho_o\, M_e} C_o$$

in which V_e is the price that someone would be willing to pay for ethanol based on equal cost for the oxygen provided, n is the number of oxygen atoms in a formula weight of an oxygenate, ρ is the density of an oxygenate, M is its molecular weight, the subscript e refers to ethanol, the subscript o refers to the competing oxygenate, and C_o is the cost of the competing oxygenate. Since all the leading oxygenates have one oxygen atom in their formulae and the densities are quite similar, the primary factor affecting the value of ethanol is the ratio of the molecular weight of the competing oxygenate to that of ethanol. Only methanol has a lower molecular weight than ethanol of the oxygenates listed in table 74, but it is not used as an additive in the United States because of its high blending vapor pressure. The lowest molecular weight of the other competing oxygenates is that of MTBE, but its molecular weight of 88 is almost twice that of ethanol at 46. When the other terms in the above relationship are included, ethanol is found to be worth 2.04 times the price of MTBE on a volumetric basis. For MTBE selling for about $0.23/liter ($0.87/gallon), ethanol is worth $0.47/liter ($1.80/gallon), far above its retail price (fig. 55). Thus, use as an oxygenate considerably enhances the value of ethanol as a blending agent.

A number of other factors must be included in determining the value and suitability of fuel additives. These include energy content, miscibility with gasoline and water, impact on the vapor pressure of the blend, impact on other components that must be removed or added and their cost, tendency to phase separate in the presence of water, and other additive attributes or problems. Evaluation of the impact of these factors on the price a blender is willing to pay for an additive is complex, often requiring incorporation of a refinery model. However, it is important to consider their effects in the final determination of the value of ethanol and other additives, in addition to the considerations discussed above.

2.2 Ethyl Tertiary Butyl Ether (ETBE)

Ethanol can be reacted with isobutylene to form ETBE. Although the Environmental Protection Agency (EPA) currently allows 12.7% ETBE blends, if ETBE were blended at 22%, each gallon of fuel would use the same amount of ethanol as a 10% direct ethanol blend. Many of the properties of ETBE are close to those of gasoline. For example, the air-fuel stoichiometric ratio, heating value, latent heat of vaporization, and solubility characteristics are similar to gasoline. The blending octane number of ETBE is about the same as for pure ethanol, and engine performance is enhanced for ETBE blends. As shown in table 74, ETBE is quite similar to MTBE except that it lowers the vapor pressure of the gasoline to which it is added.

Although similar considerations would seem to apply to ETBE as for ethanol in assessing the value of ETBE as a gasoline extender, octane enhancer, and oxygenate, ETBE has additional value as a fuel additive because of increased regulations to reduce evaporative emissions of gasoline by lowering vapor pressure and depressing ozone formation. Consideration of the expression for assessing the value of ETBE as an oxygenate compared to MTBE suggests that ETBE is worth approximately 87% of the price of MTBE. From this, we could deduce that the ethanol used to produce ETBE is worth about 70% of the price of methanol used to manufacture MTBE. With methanol selling for about $0.12/liter ($0.45/gallon), ethanol would have to sell for about $0.084/liter ($0.32/gallon) to be competitive for ETBE production, far below the current ethanol selling price (fig. 55). Yet, many major oil companies are now beginning to manufacture large trial batches of ETBE, because its reduction of vapor pressure allows them to leave more volatile and inexpensive compounds such as n-butane in the gasoline while still meeting vapor pressure requirements. In addition, it is fully miscible with gasoline, does not suffer phase separation problems, and allows reduction of aromatics content. This suggests ETBE is worth substantially more than a simple evaluation as a source of fuel oxygen would suggest.

2.3 Neat Ethanol

Ethanol is used widely as a neat fuel (nearly pure) in Brazil. In that country, hydrous ethanol containing about 95% ethanol and 5% water is used directly as the fuel for dedicated-ethanol vehicles. As a neat fuel, the price that customers are willing to pay for ethanol, A, is given by the relationship:

$$A = \eta e p$$

in which η is the relative efficiency for ethanol use compared to gasoline, e is the ratio of volumetric energy content of ethanol compared to gasoline, and p is the price of gasoline. Based on lower heating values, we can see that the energy ratio e is about 0.66 for ethanol compared to gasoline. Thus, if we assume no increase in efficiency for use of ethanol relative to gasoline, ethanol would have to sell for about two-thirds of the price of gasoline to be competitive (fig. 55). However, experience with ethanol in dedicated, optimized engines suggests that ethanol use can achieve about a 20% increase in engine efficiency relative to gasoline use because of the higher octane of ethanol, its higher heat of vaporization, and other favorable engine properties (Lynd et al. 1991a). If a value of 1.2 is utilized for η in our previous equation, the customer would be willing to pay about 83% of the price of gasoline for ethanol or about $0.13 to $0.14/liter ($0.49 to $0.53/gallon) at the plant gate (fig. 55). This price range is well below the current price of ethanol derived from corn. Thus, use of ethanol as a neat fuel requires advances in technology for ethanol production from lignocellulosic biomass or corn to bring the price to levels competitive with gasoline on the open market unless environmental concerns dictate other than simple economic criteria be applied. As a result, blending of ethanol with gasoline is more promising in the near term.

3. Technology Status

In this section, the technology for production of ethanol from corn and other starch crops as well as lignocellulosic biomass will be described. The availability of these materials and the corresponding ethanol potential will be estimated. Production of ethanol from sugar crops is not discussed because the price of sugar is too high to make it a viable feedstock for ethanol production in the United States (Commodity Research Bureau 1991).

3.1 Ethanol from Corn and Other Starch Crops

Ethanol can be produced by the breakdown of starch from corn and other grains to form sugars for fermentation to ethanol. Currently, corn is the predominant starch crop used for this purpose in the United States. Therefore, this discussion will focus on corn, although the technology could be directly applied to other starch crops such as milo or wheat.

3.1.1 Corn Composition and Availability. As shown in figure 56, corn is composed of about 70% to 75% starch, with the remaining fractions consisting of about 10% protein, 4.5% oil, and 10%–15% other materials such as fiber, ash, and sugar (Watson et al. 1987). The starch can be broken down or hydrolyzed to produce glucose sugar which can be fermented into ethanol. The non-starch fraction of corn can be converted into a variety of feed and food co-products.

Essentially all fuel ethanol produced in the United States today is made from corn by one of two processes: dry or wet milling. Ethanol production from corn has grown considerably from only about 0.1% of the gasoline sold in the country in 1981 to about 3.8 gigaliters (1 billion gallons) of ethanol or close to 1% of the gasoline market in 1992. About 8.6 dry megatonnes (400 million bushels) of corn and other starch crops are now converted into ethanol annually at about 50 fuel ethanol production facilities in the United States (U.S. Department of Agriculture 1987). It has been estimated that about 15 to 19 gigaliters (4 to 5 billion gallons) of ethanol per year could be produced from corn and other starch crops in this country utilizing about 34 to 43 megatonnes (1.6 to 2.0 billion bushels) of corn. However, the U.S. Department of Agriculture predicts that further expansion in corn production will place strong downward pressure on co-product prices while straining the ability of the agricultural community to produce such large amounts of corn, resulting in higher corn prices (USDA 1989). Thus, corn ethanol provides a significant potential for ethanol production in this country in the near term, but substantial expansion to a major share of the transportation fuel market requires consideration of other resources.

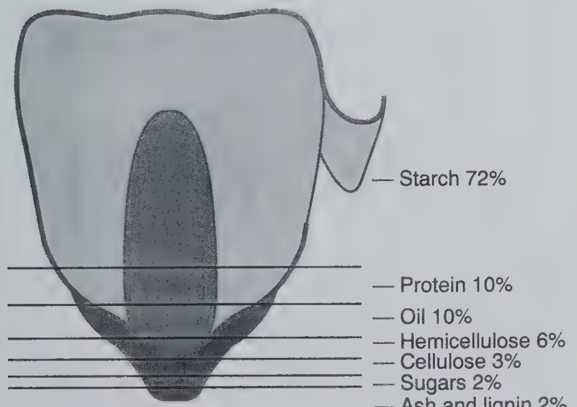


Fig. 56. Corn kernels are composed predominantly of starch with the remaining material being made up of protein, oil, fiber, ash, and sugar.

3.1.2 Ethanol Production Processes. Corn can be converted into ethanol in a dry-milling process in which the corn is first milled to a fine particle size. The wet milled corn is heated, and enzymes are added to the corn to break down the starch into the sugar glucose, which yeasts ferment into ethanol. About 440 to 458 liters of ethanol are produced per tonne (2.5 to 2.6 gallons/bushel) of corn processed in a dry-milling operation. An approximately equal weight of 340 to 360 kilograms per tonne of corn (16 to 17 pounds/bushel) of carbon dioxide evolve during fermentation for the dry-milling process. In addition, 360 to 380 kilograms per tonne of corn (17 to 18 pounds/bushel) of an animal feed co-product called distillers dried grains with solubles (DDGS) are produced. DDGS contains about 27% protein (Watson et al. 1989, Lewis and Grimes 1988). Figure 57 depicts the dry-milling process, which is geared primarily for ethanol production; about one-third of the ethanol produced in the United States is produced in dry-milling operations.

In the wet-milling process, the components of corn (oil, protein, fiber, solubles, and starch) are first separated from each other. The oil is refined to a high quality, yielding about 37 kilograms of corn oil per tonne (1.75 pounds per bushel). The protein is dried and sold as high-protein animal feed known as corn gluten meal. About 72 kilo-

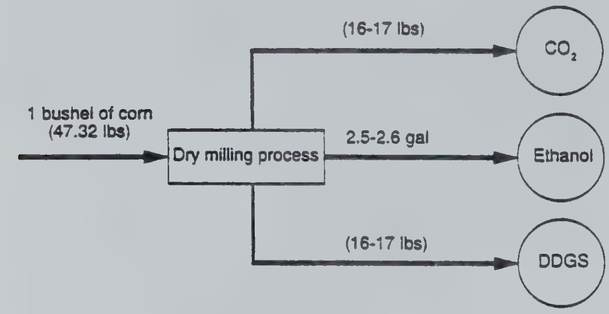


Fig. 57. Block flow diagram for dry milling of corn to ethanol with production of the animal feed co-product DDGS.

grams of this 60% protein product are produced per tonne of corn processed (3.4 pounds per bushel). The fiber and solubles are combined and sold as a low-protein animal feed, termed corn gluten feed, that contains about 21% protein; 275 kilograms of corn gluten feed result from one tonne of dry corn (13 pounds per bushel). Enzymes can convert starch to glucose to make products including high-fructose corn syrup and sweeteners such as dextrose. The glucose can also be fermented to produce about 440 liters of ethanol per dry tonne of corn (2.5 gallons per bushel) (Lewis and Grimes 1988). Figure 58 illustrates the wet-milling process as applied to ethanol production. Wet milling produces about two-thirds of the approximately 3.8 gigaliters (GL) (1.0 billion gallons) of ethanol now sold annually in the United States. However, it is important to note that not all wet-milling plants produce ethanol, and of those that do, ethanol production is often seasonal to utilize plant capacity that has been idled by lulls in demand for other starch-based products, particularly high-fructose corn syrup.

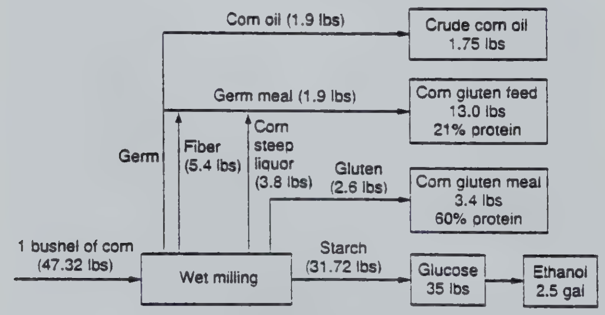


Fig. 58. Simplified schematic of the wet-milling process for production of ethanol from corn along with food-grade corn oil and the animal feed co-products corn gluten feed and corn gluten meal.

One company, Archer-Daniels Midland (ADM), produces the majority of fuel ethanol from corn in the United States and accounts for more than 55% of total U.S. capacity (Wheeler et al. 1991). Table 75 summarizes the major ethanol producers from corn and other starch crops.

3.2 Lignocellulosic Biomass Composition and Availability

Lignocellulosic biomass includes agricultural residues such as corn cobs and wheat straw, forestry wastes, industrial processing residues such as waste streams in the pulp and paper industry, a significant fraction of MSW, and woody and herbaceous plants grown as feedstocks for production of ethanol or other fuels. Although the external appearance of these many forms of biomass is quite different, the composition is very similar, as shown in figure 59. The largest fraction, typically 35% to 50%, is cellulose, a polymer of glucose that can be broken down or hydrolyzed to yield individual glucose molecules. yield individual glucose molecules. Because most of cellulose is crystalline, it is difficult to break down, but once glucose is produced, this six-carbon sugar can be readily fermented into ethanol. The second largest constituent of biomass is generally hemicellulose, comprising 20% to 30% of the material. Hemicellulose is also a polymer of sugars, but the types and distribution of sugar molecules in the polymer varies with the source of biomass. With the exception of softwoods, a five-carbon sugar known as xylose is typically the predominant component, and while hemicellulose is readily broken down to form sugars for most sources of biomass, many of the five-carbon sugars cannot be converted into ethanol with conventional fermentative organisms. The bulk of the remaining fraction of biomass (about 15% to 25%) is lignin, a phenyl-propene polymer of complex composition that cannot be fermented to ethanol. Various plant oils, proteins, and other compounds classified as extractives, plus ash, make up the rest of the biomass structure.

Table 76 summarizes the potential availability of lignocellulosic biomass within the United States. Information is presented on agricultural, forestry, and municipal wastes. Estimates are also given on the quantities of lignocellulosic biomass that could be grown as energy crops on idle, excess, and potential cropland as well as forest land. This table includes targets for biomass productivities along with the projected availability of land. From this

Table 75

U.S. producers of ethanol from corn (Wheeler et al 1991)

COMPANY	PLANT LOCATION	CAPACITY (MMgal/yr)	START-UP DATE	FEEDSTOCK	BY-PRODUCTS	MARKETS
American Diversified Corporation	Hastings, NE	13	1984	Corn, milo	DDGS	Fuel only
Archer-Daniels Midland Company	Cedar Rapids, IA	700 (for all ADM facilities)		Corn	CO_2, corn oil, gluten feed and meal	Fuel & Industrial
	Clinton, IA					Fuel & Industrial
	Decatur, IL					Fuel & Industrial
	Peoria, IL			Corn	DDGS	Fuel only
Biocom USA Ltd.	Jennings, LA	40				ETBE only
CENEX Agrifuels Co.	Walhalla, ND	11	1985	Barley, corn	DDGS, CO_2	Fuel only
Grain Processing Corporation	Muscatine, IA	60	1942	Corn	DDGS, CO_2	Industrial & Beverage
H.J. Heinz Company (Roquette)	Keokuk, IA	11	1988	Corn	Corn, gluten feed, corn gluten meal, & CO_2	Fuel only
High Plains Corporation	Colwich, KS	10	1985	Milo, corn	DDGS, livestock feed, CO_2	Fuel only
Kentucky Agricultural Energy Corporation (4)	Franklin, KY	(21)	1982	Corn	DDGS, CO_2	Fuel only
Midwest Grain Products, Incorporated	Atchison, KY	22	1942	Corn, milo, wheat	CO_2, DDGS	Beverage, fuel & industrial
	Pekin, IL	19	1980	Corn, milo, wheat	CO_2, DDGS	Beverage, fuel & industrial
New Energy Company of Indiana	South Bend, IN	63	1984	Corn	CO_2, DDGS	Fuel only
Pekin Energy	Pekin, IL	80		Corn		Primarily fuel
Portales Energy Company, Inc.	Portales, NM	10	1985	Corn, sorghum	CO_2	Fuel only
South Point Ethanol	South Point, OH	60	1982	Corn	DDGS, CO_2	Fuel only
A.E. Staley Manufacturing Company	Loudon, TN	60	1982	Corn	Cornstarch, corn oil, corn gluten feed	Primarily fuel; small amounts of industrial & beverage
Tennol Energy Company	Jasper, TN	(25)	1986	Corn	DDGS, CO_2	Fuel only

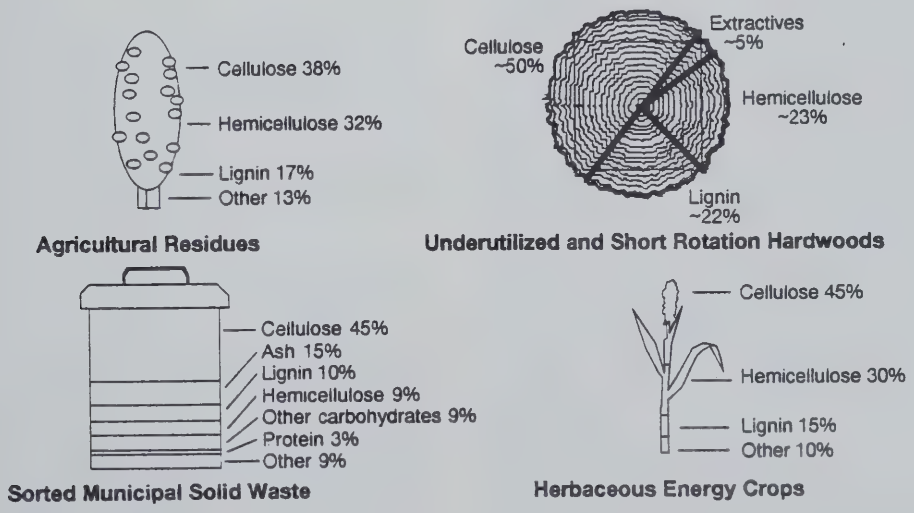


Fig. 59. The major fraction of the various forms of lignocellulosic biomass is cellulose, with hemicellulose being the second largest component for most biomass sources. Lignin, extractives, and ash comprise the remainder of these materials.

Table 76. Potential availability of lignocellulosic biomass and the corresponding ethanol production (Lynd et al. 1991a)

	Productivity		Land Available		Biomass Availability		Ethanol Potential		Energy Potential	
	Tonnes/ Hectare/Yr	Tons/ Acre/Yr	10^6 Hectares	10^6 Acres	Megatonnes	10^6 Tons	GL	Billions of Gallons	GJ[b]	Quads[b]
Waste Materials										
- Agricultural					203	224	84.8	22.4	1.8×10^9	1.7
- Forestry					167	184	69.6	18.4	1.5×10^9	1.4
- MSW					111	122	34.8	9.2	7.4×10^8	0.7
Lignocellulosic Biomass										
- Cropland										
Idled (1988)[a]	11/22	5/10	32	78	354-707	390-780	149.5-293.7	39.5-77.6	3.2×10^9-6.2×10^9	3.0-5.9
Excess (2012)[a]	11/22	5/10	61	150	680-1361	750-1500	283.9-567.8	75.0-150.0	6.0×10^9-1.2×10^{10}	5.7-11.4
Potential	7/18	3/8	61	150	408-1088	450-1200	169.2-453.4	44.7-119.8	3.6×10^9-9.6×10^9	3.4-9.1
- Forest Land	7	3	39	96	263	290	109.4	28.9	2.3×10^9	2.2
Total			132-161	324-396	1506-3193	1660-3520	617.3-1319.8	163.1-348.7	1.3×10^{10}-2.8×10^{10}	12.4-26.5

[a] Values are for biomass production potential in 1988 and 2012 based on expected availability of land and current and future biomass production (Lynd et al. 1991a).

[b] Ethanol rated at its lower heating value without consideration for possible efficiency improvements that would result in displacement of greater quantities of gasoline.

information, the potential supply of biomass is derived. For waste streams, these values are estimated from the potentially collectable fraction of such materials based on other studies. The potential amount of ethanol that could be produced and its energy impact are calculated from the biomass estimates based on the information described in the paper by Lynd et al. (1991a).

It is evident from this table that on the order of 190 gigaliters (50 billion gallons) of ethanol could be produced annually from waste materials alone. Production of about 510 gigaliters (140 billion gallons) per year of ethanol would be required to replace the current annual gasoline market of approximately 410 gigaliters (110 billion gallons) because of the slightly lower volumetric energy content of ethanol fuels. Therefore, the amount of ethanol that could be produced from waste materials would not be adequate to replace all gasoline use in the country. However, when we include the amount of ethanol that could be derived from energy crops, the total amount of ethanol potentially available could be far more than required to displace all gasoline use. Thus, ethanol from lignocellulosic biomass presents a substantial potential for major displacement of fossil fuels in this country.

3.3 Acid Hydrolysis of Lignocellulosic Biomass

Over the years, a number of processes have been studied for converting lignocellulosic biomass into ethanol catalyzed by dilute or concentrated acid. As illustrated in figure 60, the biomass is reduced in size to facilitate acid diffusion into the biomass in a pretreatment step. The cellulose fraction is hydrolyzed by the acids to produce glucose, which can be fermented into ethanol. The soluble xylose and most of the other sugars derived from hemicellulose by the acid-catalyzed hydrolysis reaction can also be fermented to ethanol, and the lignin can be burned as fuel to power the rest of the process, converted to octane boosters, or used as feedstocks for the production of chemicals.

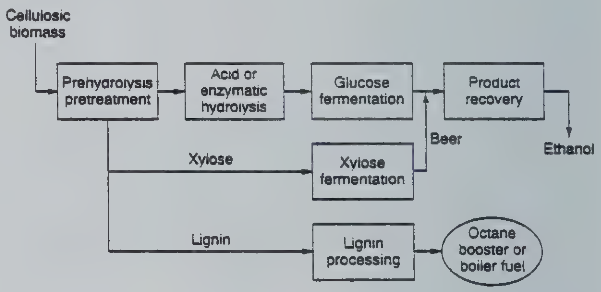


Fig. 60. Generalized process flow diagram for conversion of lignocellulosic biomass to ethanol by acid- or enzyme-catalyzed hydrolysis of cellulose.

At dilute acid concentrations, high temperatures of about 200 to 240 °C (390 to 460 °F) are required to hydrolyze the cellulose to sugars (Wright 1983 and 1988). Unfortunately, these conditions are also severe enough to degrade glucose into substantial quantities of hydroxymethyl furfural (HMF), which can in turn form tars. Similarly, xylose degrades to furfural and tars. Substantial formation of degradation products can not be avoided at the harsh conditions required for dilute acid hydrolysis, so the degradation products must be sold as coproducts to achieve favorable economics. However, markets for these products are not sufficient to complement large-scale ethanol production (Gaines and Karpuk 1987). Acid-catalyzed processes provide a near-term technology for production of fuel-grade ethanol from lignocellulosic biomass, but the low ethanol yields (50%–70%) and limited co-product markets typical of dilute acid systems make these processes unable to compete with existing fuel options in the long term (Wright 1983 and 1988).

Several dilute acid hydrolysis pilot plants were constructed in the United States during World War II as part of an effort to produce ethanol for fuel use, but the economics were unfavorable to continue operation in a free market economy. Dilute acid-catalyzed processes are currently operated in the Soviet Union for converting lignocellulosic biomass into ethanol and single cell protein (Wenzl 1970). In this country, the Tennessee Valley Authority (TVA) has a pilot plant for converting MSW to ethanol using dilute acid hydrolysis (Bulls et al. 1992).

Halogen or concentrated sulfuric acid processes can be carried out at near ambient temperatures, and little if any sugar degradation results (Goldstein and Easter 1992, Goldstein et al. 1983). Therefore, they achieve the high yields essential to economic viability. However, because low-cost acids (e.g., sulfuric) must be used in large amounts while more potent halogen acids are relatively expensive, recycle of acids by efficient low-cost recovery operations is vital to achieve economic operation. Unfortunately, the acids must also be recovered at a cost substantially lower than that of producing these inexpensive materials in the first place (Wright et al. 1985). Concentrated acid technology is being offered for conversion of low-cost materials such as MSW into ethanol (Goldstein and Easter 1992), but the prospects for further cost reductions appear limited.

3.4 Enzymatic Hydrolysis of Lignocellulosic Biomass

Instead of acids, cellulase enzymes catalyze the breakdown of cellulose into glucose for subsequent fermentation to ethanol, as shown in figure 60. Enzyme-catalyzed processes achieve high yields under mild conditions with relatively low amounts of catalyst. Because enzymes are highly selective in the reactions they catalyze, by-products such as those accompanying dilute acid hydrolysis are not formed, and treatment of wastes is reduced. Enzymes are also biodegradable and environmentally benign. Over the years, several enzyme-catalyzed processes have been studied in the laboratory, but only a few investigations have been taken to a larger scale. Recent advances in enzymatic technology have reduced the costs of ethanol production to the point that large-scale operation appears economically viable, and larger scale operation is warranted to prove process performance. For more details on technology for both enzymatic and dilute acid catalyzed processes for conversion of lignocellulosic biomass into ethanol than can be offered here, the reader is referred to a chapter by Schell et al. (1992).

3.4.1 Pretreatment. Lignocellulosic biomass is naturally resistant to enzymatic attack, and a pretreatment step is required to open up the structure and overcome this resistance if the enzyme-catalyzed hydrolysis process is to proceed at acceptable rates and yields. Several options have been considered for biomass pretreatment including steam explosion (Brownell and Saddler 1984, Brownell et al. 1986), acid-catalyzed steam explosion (Clark and Mackie 1987), ammonia fiber explosion (Holtzapple et al. 1990, Dale and Moreira 1982, Dale et al. 1985), organosolv (Chum et al. 1985), supercritical extraction (Chou 1986, Reyes et al. 1989), and dilute acid. At this time, the dilute sulfuric acid process appears to be an attractive near-term option with economic potential (Schell et al. 1991, Knappert et al. 1980 and 1981). In this process, about 0.5% sulfuric acid is added to the feedstock, and the mixture is heated to around 140 to 160 °C for 5 to 20 minutes (Grohmann et al. 1985 and 1986; Torget et al. 1990). Under these conditions, most of the hemicellulose is broken down to form xylose and other sugars, leaving a porous structure of primarily cellulose and lignin that is more accessible to enzymatic attack. Evaluation of the dilute acid process with various agricultural residues, short-rotation hardwoods, and herbaceous energy crops has consistently shown that the conversion yields correlate well with the degree of hemicellulose removal (Grohmann et al. 1986; Torget et al. 1988, 1990 and 1991). Although this process has good near-term potential, significant benefits would result if a low-cost scheme could be devised that would also remove lignin, because the solid lignin associated with the cellulose creates some processing difficulties in the fermentation step. In addition, it would be useful to employ a catalyst that does not require neutralization with formation of salts.

3.4.2 Enzyme Production. Several organisms, including bacteria and fungi, produce cellulase enzymes that can be used to hydrolyze cellulose into glucose sugar. Currently, genetically altered strains of the fungus Trichoderma reesei are generally favored for cellulase production because relatively high yields, productivities, and specific activities of cellulase are realized. The best performance is usually achieved in the fed-batch mode of operation in which lignocellulosic biomass is metered into the fermenter during the growth of the fungus and the production of cellulase (Watson et al. 1984). Simple batch production of cellulase with the addition of all ingredients at the beginning of the enzyme production cycle may also be used. Continuous enzyme production has typically suffered from lower cellulase productivities (Hendy et al. 1984).

3.4.3 Cellulose Hydrolysis and Glucose Fermentation. Three approaches have received the most attention for conversion of the cellulose fraction into ethanol: separate hydrolysis and fermentation, simultaneous saccharification and fermentation, and direct microbial conversion.

- Separate Hydrolysis and Fermentation (SHF)

In the SHF process, the lignocellulosic biomass is first pretreated to open up the biomass structure and facilitate subsequent processing. A small portion of the pretreated biomass is added to an enzyme production vessel to support growth of a fungus or other microorganism that releases cellulase enzyme. The cellulase is then added to the bulk of the pretreated substrate in a hydrolysis reactor, catalyzing the breakdown of the cellulose to glucose. The resulting sugar stream passes to a fermenter, where yeast or other microorganisms convert the glucose into ethanol (Mandels et al. 1974, Wilke et al. 1976).

- Simultaneous Saccharification and Fermentation (SSF)

The production of cellulase is virtually the same for the SSF process as for SHF. However, for the SSF approach, hydrolysis and fermentation are combined in one vessel. The presence of yeast with the cellulase minimizes the accumulation of glucose in the vessel. Because glucose slows down the action of current cellulase enzymes, higher ethanol production rates, yields, and concentrations are possible for SSF than SHF (Gauss et al. 1976, Takagi et al. 1977, Ghosh et al. 1982).

Over the last several years, a number of studies have identified combinations of cellulase enzymes and yeast to speed the rate of conversion of lignocellulosic biomass to ethanol (Spindler et al. 1988, 1989, 1990 and 1991; Wyman et al. 1986; Lastick et al. 1989). Figure 61 illustrates the results of conversion of lignocellulosic biomass into ethanol for selected feedstocks with the SSF process and the SHF process. As shown for each of the feedstocks, the SSF approach achieves much higher yields of ethanol at the same enzyme loading than the SHF approach. As illustrated in figure 62, cellulase is a mixture of enzyme components designated as endoglucanase, exoglucanase, and β-glucosidase. Endoglucanase breaks the cellulase chain somewhere along its length while exoglucanase breaks off sugar dimers called cellobiose from the end of the chain. β-glucosidase then converts the cellobiose into glucose molecules for fermentation to ethanol. Cellobiose is a powerful inhibitor of cellulase enzyme, particularly the exoglucanase component of figure 62, and it appears that adding β-glucosidase minimizes the accumulation of cellobiose in the fermentation broth. Therefore, higher yields are achieved when the β-glucosidase is added to the fermentation broth than when it is not. Similar benefits have been found by employing cellobiose-fermenting yeast or cellulase enzyme with greater β-glucosidase activity typical of many modern formulations.

Seven or eight years ago, it required on the order of 2 weeks to convert the cellulose into ethanol in an SSF process at yields of approximately 70% (Lastick et al. 1984). By selection of cellulase with enhanced characteristics, such as higher levels of β-glucosidase, as well as selection of yeasts that perform well under SSF conditions, on the order of 90% to 95% of the cellulose entering the SSF process can be converted into ethanol in about 3–7 days for a variety of feedstocks (Spindler et al. 1990 and 1991).

- Direct Microbial Conversion (DMC)

The DMC process combines the enzyme production, cellulose hydrolysis, and sugar fermentation steps in one vessel (Veldhuis et al. 1936; Ng et al. 1977; Garvey et al. 1978; Lynd et al. 1989). In the most tested configuration, two bacteria are employed, one that produces cellulase enzymes and ferments glucose formed by the breakdown of cellulose while the other ferments the five-carbon sugars from hemicellulose into ethanol. Unfortunately, the bacteria also produce a number of

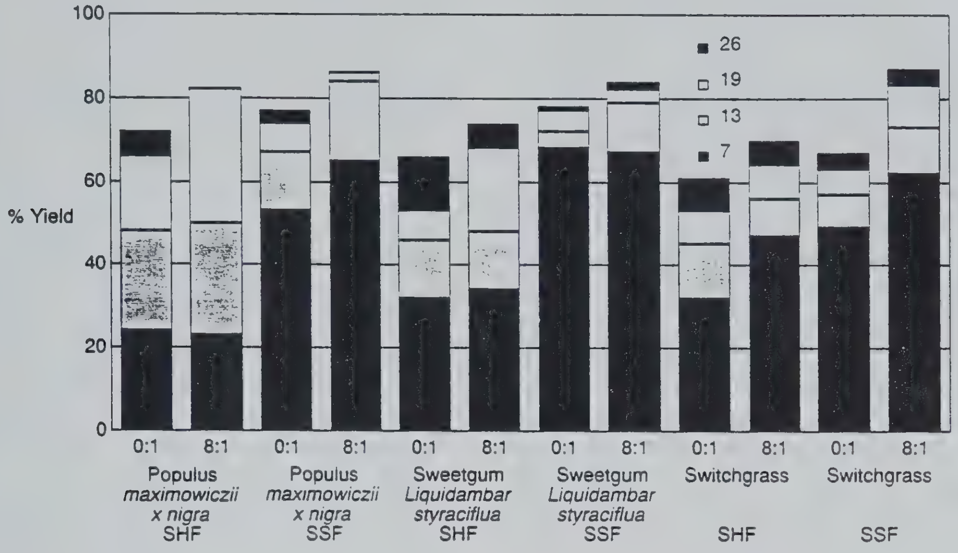


Fig. 61. Comparison of theoretical ethanol yields of cellulose to ethanol from the SSF and SHF processes with different substrates, cellulase concentrations (7, 13, 19, and 26 International Units/gram of substrate), and with (8:1) and without (0:1) β-glucosidase supplementation.

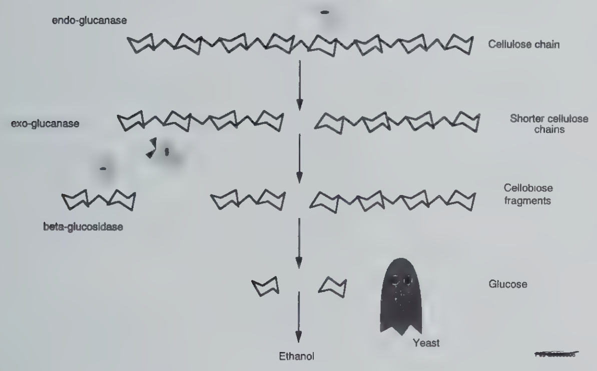


Fig. 62. Cellulase is a mixture of enzymes known as endoglucanase, exoglucanase, and β-glucosidase that act synergistically to break down cellulose into glucose that yeast can ferment into ethanol.

products in addition to ethanol, and yields are currently lower than for SHF or SSF processes. There is evidence that yields could be increased by process modifications (Lynd et al. 1991b). The bacteria are also not very tolerant to ethanol, and a dilute ethanol product results. If efforts to enhance ethanol yields are successful, the DMC approach could be the most attractive due to several advantageous features such as reduced capital cost for fermenters and lower power requirements.

At this time, the SSF approach is generally favored for ethanol production because it achieves higher rates, yields, and concentrations of ethanol than the SHF or DMC options (Wright 1988, Wright et al. 1988). High yields increase revenue while reducing waste treatment costs, and higher rates and concentrations lower capital and operating costs. In addition, about half as many fermenters are needed as for the SHF approach, further reducing capital and operating costs. The presence of ethanol in the fermentation broth reduces the possibility of contamination by unwanted microbes. Other approaches may be developed in the future to achieve similar or better performance than SSF.

3.4.4 Hemicellulose Conversion. The hemicellulose polymers in lignocellulosic biomass such as hardwoods, agricultural residues, and herbaceous plants can be readily broken down to form xylose and other sugars during the dilute acid pretreatment step (Grohmann et al. 1985). However, until recently, five-carbon sugars such as xylose could not be effectively utilized, and it was necessary to send these materials to waste disposal or find a suitable coproduct application, such as furfural. From an economic perspective, this costs the process twice: first, we are throwing away the xylose we paid for as part of the feedstock and second, the cost of waste disposal for such a major fraction of the feedstock inflicts a large economic penalty on the process. Several options, outlined below, have been examined for xylose utilization.

- Conversion of Xylose into Furfural

For dilute acid-catalyzed breakdown of cellulose to fermentation sugars, a significant fraction of the xylose degrades into furfural (Brennan et al. 1986; Kwarteng 1983; Wright 1988c). Similarly, the xylose left after pretreatment can also be reacted to furfural by heating with acid. This product is currently manufactured for use in foundry and other applications, so it could be sold as a co-product, generating additional revenues. However, the furfural market would be quickly saturated by the volume of furfural that would accompany large-scale fuel ethanol production (Gaines and Karpuk 1987). Thus, although furfural sales could prove valuable for initial introduction of a few ethanol plants, it would not support the commercialization of a large ethanol industry.

- Yeast for Ethanol Production from Xylose

Another avenue is to use certain strains of yeast that are known to ferment xylose into ethanol, such as Candida shehatae, Pichia stipitis, and Pachysolen tannophilus (Skoog and Hahn-Hager 1988; Prior et al. 1989; Jeffries 1990). These strains require small amounts of oxygen (microaerophilic operation) in the fermentation broth to ferment xylose (Grootjen et al. 1990; Ligthelm et al. 1988). Large-scale production of ethanol fuels will probably require the use of huge fermenters with volumes approaching a million gallons each, and proper control of oxygen in such large vessels could be difficult. These yeast strains typically cannot yet achieve as high ethanol yields, rates, or tolerance as conventional strains that ferment glucose. Improvements in such strains could result in economic application for xylose conversion to ethanol.

- Other Microorganisms for Ethanol Production

Other microorganisms, such as thermophilic bacteria and fungi, can anaerobically ferment xylose into ethanol (Carreira et al. 1983; Christakopoulos 1991; Lacis and Lawford 1988 and 1989; Lynd 1989, Buchert et al. 1989; Antonopoulos and Wene 1987; Asther and Khan 1984; Slapack et al. 1987). Ethanol tolerance has not been satisfactorily demonstrated for bacteria, although some new evidence suggests previous conclusions may have been premature (Lynd et al. 1991b). Historic data suggest that ethanol yields are low, but new information indicates that the yields could be improved in continuous culture. The fungi evaluated currently suffer from similar limitations in both ethanol tolerance and yield.

- Simultaneous Isomerization and Fermentation of Xylose to Ethanol

Several groups have studied the use of xylose isomerase enzyme to convert xylose into an isomer called xylulose that many yeast can ferment into ethanol under anaerobic conditions (Jeffries 1981; Chaing et al. 1981; Tewari et al. 1985). Researchers have genetically engineered the common bacteria Escherichia coli to produce large quantities of xylose isomerase for such a process, and ethanol yields of 70% of theoretical have been achieved in the simultaneous isomerization and fermentation of xylose process (Lastick et al. 1990). In this configuration, the enzyme and yeast are employed together to drive the equilibrium-limited fermentation to near completion, with the primary yield loss resulting from xylitol formation. This process has the advantage of employing anaerobic yeast that are easier to use at a large scale, but the need to provide xylose isomerase enzyme and adjust for differences in pH optima between the yeast and enzyme complicate the technology.

- Genetically Altered Bacteria

Researchers at the University of Florida have successfully introduced the genes from the glucose fermenting bacterium Zymomonas mobilis into the common bacterium E. coli so that the latter can now ferment xylose directly into ethanol (Ingram and Conway 1988; Ingram et al. 1987). This group has also successfully applied this approach to other bacteria including Klebsiella oxytoca (Wood and Ingram 1992; Ohta et al. 1991; Burchhardt and Ingram 1992). As a result, a single organism can ferment xylose as well as other sugars, and data suggest high yields are possible. However, these bacteria require operation at near neutral pH while production of byproduct acids could drive the pH down, requiring addition of bases to control the pH. These genetically engineered bacteria are a very promising approach to five-carbon sugar utilization.

Full integration of these technologies into the overall conversion process is required to evaluate and improve their performance. Advantages could also result by genetic modifications or other approaches.

3.4.5 Lignin Utilization. Lignin generally represents the third largest fraction of lignocellulosic biomass and is often present in similar quantities to the hemicellulose fraction. Thus, it is important to derive value from lignin if economic ethanol production is to be achieved. Three options, discussed below, lead the possibilities for lignin use.

- Use as a Boiler Fuel

  Lignin has a high energy content and can be used as a boiler fuel (Wright 1988c; Hinman et al. 1992; Domalski et al. 1987). The amount of lignin in most feedstocks is more than enough to supply all the heat required for the entire ethanol conversion process, plus generate enough electricity to meet its electrical demands. In fact, excess electricity beyond all of these needs is generated, and additional revenue can be generated from electricity exports from the plant (Hinman et al. 1992; Chem Systems 1990). The electricity sold for current plant designs is equivalent to about 8% of the fuel value of the ethanol product, and greater revenues are likely as the technology is improved to require less process heat and electricity.

- Production of Octane Boosters

  Lignin is a complex phenolic polymer that can be broken down to form a mixture of monomeric phenolic compounds and hydrocarbons (Johnson et al. 1990). The phenolic fraction can be reacted with alcohols to form methyl or ethyl aryl ethers, which are good oxygenated octane boosters. Because octane boosters are more valuable than boiler fuel, this option for lignin use would generate more revenue. However, the technology must be improved to provide high product yields, and the conversion costs must be low enough to provide a net income gain for the ethanol plant.

- Production of Chemicals from Lignin

  A number of chemicals could be produced from lignin including phenolic compounds, aromatics, dibasic acids, and olefins (Busche 1985). Such materials could have a high value that would augment the total revenue for the ethanol plant. However, just as for the conversion of lignin into octane boosters, the cost of the conversion process must be low enough to ensure a net income gain. In addition, high yields of target products will likely be necessary to achieve economic viability. The spectrum of products that could be derived from lignin must have sufficient market volume to match the expected output for large-scale use of ethanol technology or lignin use will only support a few ethanol plants (Gaines and Karpuk 1989).

3.4.6 Ethanol Recovery. About a 3% to 12% solution of ethanol in water is produced in the fermentation process, with the exact concentration determined by the substrate, fermentative microorganism, enzyme, and process configuration. In addition, yeast, inerts such as lignin, enzymes, unreacted carbohydrates, and various salts remain in the broth. In most commercial applications, the entire mixture is fed to a distillation (beer) column that concentrates the ethanol in the overhead product while allowing the solids and water to exit from the bottom. The enriched ethanol stream passes to a second distillation (rectification) column for concentration to the ethanol-water azeotrope of about 95% by weight ethanol. To use ethanol as a hydrous fuel, this azeotropic mixture is suitable without further processing (Hinman et al. 1992; Chem Systems 1990), provided the appropriate distribution infrastructure is available.

Water has a low miscibility in gasoline, and almost all the water must be removed from ethanol that will be blended with gasoline. To break the ethanol-water azeotrope, a third component such as benzene or cyclohexane can be added to allow purification of ethanol by tertiary distillation. Alternatively, molecular sieves such as corn grits can be used to preferentially adsorb the ethanol or water. Membranes can also be used that are permeable to one of the components, typically water, while retaining the other by a technology called pervaporation. At this time, distillation with a third component and molecular sieves are favored commercially.

4. Energy Balance and Impact on Carbon Dioxide Accumulation

Energy costs can be an important element in the economics of a process. In addition, the impact of ethanol technology on displacement of imported oil depends on the amounts and types of energy used by the process. Considerable controversy and confusion exists about how to interpret this information for energy efficiency and the impact on the potential for global climate change. Energy inputs must be accounted for and the performance of ethanol must be properly compared to that for fossil fuels if comparisons are to be made among fuels.

4.1 Energy Use

Figure 63 summarizes energy flows for the production of ethanol from lignocellulosic biomass (Lynd et al. 1991a). Modest energy inputs are required to grow lignocellulosic biomass because cultivation and fertilizer needs are not large. In addition, no process energy input is shown because the lignin contained in the feedstock can be used as a boiler fuel, and the amount of energy contained in the lignin is sufficient to produce process heat and electricity for the overall process. The equivalent of about 8% of the ethanol fuel value can be sold as electricity based on current technology (Chem Systems 1990; Hinman et al. 1992), thereby displacing about three times that amount of fossil energy inputs for electricity production by power companies.

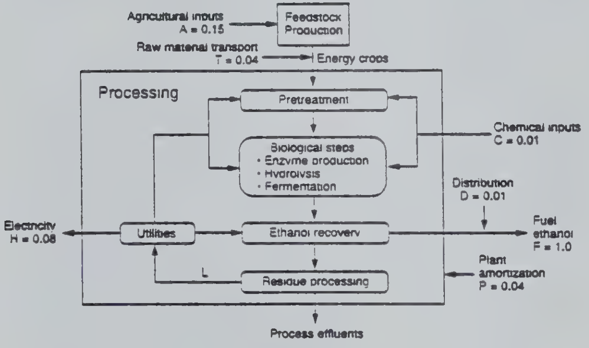


Fig. 63. Energy requirements and outputs for production of ethanol from lignocellulosic biomass based on one unit of ethanol energy output.

If the amount of fossil energy inputs are totaled for current technology (Chem Systems 1990), about 5.3 megajoules/liter (19,000 Btu/gallon) of ethanol are required for ethanol production from lignocellulosic biomass, as shown in table 77. Alternatively, three times the electricity produced could be subtracted from the fossil fuel requirements to account for the fossil fuel that would be used in any event for producing that quantity of electricity (Ho 1989). In this case, the net amount of fossil fuel use, as shown in table 77, is only about 0.2 megajoules/liter (700 Btu/gallon) of ethanol. For comparison, fossil sources account for about 3.9 megajoules/liter (11,000 Btu/gallon) of gasoline produced. Gasoline has a lower heating value of about 32 megajoules/liter (115,000 Btu/gallon), compared to ethanol at 21 megajoules/liter (76,000 Btu/gallon).

One measure of the efficiency of ethanol production is to calculate the ratio R defined as the amount of energy produced by the process compared to the amount of fossil fuel used (Lynd et al. 1991a):

$$R = \text{Energy Outputs/Fossil Energy Inputs.}$$

In this case, the fuel value of the ethanol is added to three times the amount of excess electricity sold (to account for the thermal energy displaced), and the quantity is divided by the total fossil fuel inputs. Based on the information in table 77, ethanol fuel and thermal energy outputs are about five times greater than the total fossil fuel inputs for current lignocellulosic biomass conversion technology. Of course, if fuels and fertilizers derived from renewable resources were used in place of the fossil sources assumed in this analysis, R would become virtually infinite.

An alternative approach to measuring energy efficiency is to calculate the ratio ER of the energy in the products less external energy inputs to the energy content of the feedstock (Wyman et al. 1992);

$$ER = \frac{\text{Energy in Products} - \text{External Energy Inputs}}{\text{Energy in Feedstocks}}.$$

For current technology for ethanol production from lignocellulosic biomass with exported electricity weighted by a factor of three to account for the

Table 77. Energy inputs and carbon dioxide released in ethanol production from lignocellulosic biomass

Process	Feedstock Production	Raw Material Transport	Chemical Inputs	Process Energy	Plant Amortization	Fuel Distribution	Total Fossil Use	Coproduct Displacement of Fossil Fuel[1]	Net Fossil Fuel
Assumed Fossil Fuel	Natural Gas	Petroleum	Natural Gas	None	Natural Gas	Petroleum	--	--	--
MJ/L Ethanol	3.2	0.84	0.22	--	0.84	0.22	5.3	5.1	0.22
Carbon Dioxide Released g/L	180	60	12	--	48	12	310	550	-240

[1] Calculated on the basis of the exported electricity displacing coal-generated electricity, at 33% efficiency.

amount of thermal energy displaced and accounting for the energy required to grow biomass, this ratio is equal to about 0.43. For improvements in the technology, the ratio ER becomes about 0.56 (Wyman et al. 1992).

It is important to note that although fermentation of sugars to ethanol results in the release of almost as much carbon dioxide as ethanol produced by weight, nearly all of the energy from the cellulose and hemicellulose fractions remains in the ethanol product formed (Wyman and Hinman 1990). Thus, the conversion process concentrates the energy from the solid biomass into a liquid form more compatible with our transportation infrastructure, and since the value of both the feedstock and the product should be assessed on an energy content basis, the weight loss is actually beneficial. The main loss of feedstock energy as measured by eq (7) is the thermal energy of the lignin needed to drive the conversion process and secondarily the fraction of cellulose and hemicellulose that is not converted into products. Reductions in the need for process energy will therefore greatly improve this measure of efficiency.

4.2 Carbon Dioxide Released

The contribution of ethanol production to carbon dioxide accumulation in the atmosphere can be estimated by weighing the quantities of fossil fuels used according to the amount of carbon dioxide released by each. For the purposes of this discussion and with reference to figure 63, natural gas is assumed to be the fuel source for agricultural (A), chemical (C), and plant amortization (P) inputs; petroleum is assumed for transportation (T) and distribution (D). Coal is assumed to be the fuel used for conventional electricity generation. Combining carbon dioxide release data for these sources with the energy requirements presented in figure 63 gives the results presented in table 77 for ethanol derived from lignocellulosic biomass. Only carbon dioxide produced by combustion of fossil fuels is included because carbon dioxide generated during fermentation of biomass cellulose and hemicellulose and combustion of lignin, ethanol, and other biomass fractions would be recycled to grow new biomass to replace that harvested for energy production.

It is interesting to note that if the equivalent carbon dioxide release for production of electricity by coal is subtracted from the fossil fuel sources for ethanol production from lignocellulosic biomass, a negative carbon dioxide contribution results (table 77). This outcome is due to the low usage of fossil fuels for conversion of lignocellulosic biomass to ethanol and the displacement of fossil-generated electricity in the grid. To produce an equivalent amount of electricity from coal would actually produce more carbon dioxide than the total net released during ethanol production, and subtracting the amount of carbon dioxide that would have resulted anyway for generation of that quantity of electricity by coal gives a net credit of 0.24 kilograms of CO_2/liter of ethanol produced (2.0 pounds/gallon).

From the data in table 77, it appears that production of ethanol from lignocellulosic biomass would be a minor contributor of carbon dioxide to the atmosphere, because all of the process heat is produced by combustion of lignin, a renewable feedstock. In addition, limited fossil fuel inputs are needed to grow lignocellulosic biomass. Furthermore, biomass sources of fuels and fertilizers could be substituted for the fossil fuels assumed in this analysis, resulting in no carbon dioxide release from fossil sources for ethanol from lignocellulosic biomass. By way of comparison, gasoline use releases a total of 82 kilograms of CO_2/gigajoule (190 pounds CO_2/million Btu) or 2.61 kilograms/liter (22 pounds/gallon).

4.3 Ethanol Utilization

To compare carbon dioxide release between ethanol and fossil fuels, it is important to establish the relative amounts of fuel required to travel equivalent distances with each fuel. In the United States, ethanol is typically blended with gasoline at 10% concentrations. As mentioned earlier, the energy content of ethanol is 21 megajoules/liter (76,000 Btu/gallon); gasoline contains about 50% more energy at 32 megajoules/liter (115,000 Btu/gallon). By accounting for each of these factors, the energy content of the blend is about 31 megajoules/liter (110,000 Btu/gallon). If the range of a vehicle is assumed to be proportional to the energy density of the fuel, 1.036 volumes of blend would be required to travel the same distance as one volume of gasoline. On the other hand, data from Southwest Research Institute (Tosh et at. 1985) as well as others have shown that there is no statistically significant difference in the mileage for a 10% blend versus that of regular gasoline. In effect, this evidence suggests that the ethanol blended with gasoline has an energy density equivalent to 32 megajoules/liter (115,000 Btu/gallons).

Use of neat ethanol can be considered in at least two different ways. First, the amount of one fuel needed to travel the same distance as for another fuel can be determined by the ratio of the lower heating values of the two fuels. Thus, about 50% more ethanol would be required than for gasoline to give the same service. For an engine designed for gasoline use with only modifications in timing and air-to-fuel ratio to allow combustion of ethanol, ethanol fuel would give such a range. However, because ethanol has more favorable fuel properties such as a higher octane and heat of vaporization than gasoline, an engine optimized for ethanol can be 20% to 30% more efficient than a gasoline engine (Lynd et al. 1991a, Wyman and Hinman 1990). Assuming the latter results in a ethanol driving range of about 80% of that of gasoline on a volumetric basis.

4.4 Comparisons of Fossil Fuel Use and Carbon Dioxide Release

Table 78 presents a comparison of the fossil fuel requirements for ethanol from lignocellulosic biomass and gasoline. Consideration is given to blends and neat fuel use and to comparison of the amount of ethanol required based on lower heating value and probable distance traveled on an equal volume. The lower end of the range shown is with credit given for fossil fuel displacement for electricity production, while the higher end does not account for excess electricity production. Blends of ethanol from lignocellulosic biomass with gasoline always yield lower fossil fuel use than gasoline alone. Furthermore, for neat fuel markets, ethanol production from lignocellulosic biomass requires one-fifth or less fossil fuel inputs than gasoline, depending on the accounting given for electricity production and the assumed efficiency of ethanol utilization.

Table 78. Fossil fuel use and carbon dioxide released for ethanol from lignocellulosic biomass

Form of Fuel Use	Fossil Fuel Used (MJ/L of Gasoline Equivalent)	CO_2 Released[1] (kg CO_2/L of Gasoline Equivalent)
10% Blends Based on Lower Heating Value	33.6 - 34.1	2.40/2.47
10% Blends at Same Range as Gasoline	32.4 - 32.9	2.33/2.39
Neat Ethanol Fuel Based on Lower Heating Value	0.33 - 8.0	-0.36/0.47
Neat Ethanol Fuel Based on Improved Efficiency	0.28 - 6.6	-0.30/0.38
Gasoline	36.0	2.61

[1] First value is dervied by subtracting equivalent carbon dioxide released by coal fired electric plant, second value is for all carbon dioxide assigned to ethanol production.

Also presented in table 78 is the amount of carbon dioxide released when a vehicle is propelled the same distance by ethanol as gasoline. Again, based on the low use of fossil fuels in production of ethanol from lignocellulosic biomass, this fuel scores very well in minimizing carbon dioxide emissions that could contribute to global climate change. If we subtract the carbon dioxide emissions that would have resulted from coal to generate the amount of electrical energy exported from the ethanol plant, the net effect is that ethanol reduces carbon dioxide accumulation. It may be more appropriate to assign the carbon dioxide released to both electricity and ethanol based on the relative energy contributions and compare each to the alternative, but the benefits would still be substantial.

5. Ethanol Economics

Economics for ethanol production from starch crops and lignocellulosic biomass will both be summarized. Three important elements influence the overall economics: feedstock price, operating costs, and annualized capital charges. Each of these elements are discussed in the following sections.

5.1 Corn Ethanol

The cost of ethanol production from corn is influenced substantially by the price of corn and the price at which co-products can be sold. Therefore, these factors are considered first. Then, the capital and operating costs for a corn ethanol plant are combined with corn prices and revenues from co-products to predict the selling price of ethanol that is required to achieve a target rate of return on capital invested.

5.1.1 Corn and Co-Product Prices. Table 79 presents the historical variation in prices of corn and co-products derived from dry- and wet-milling processes, during the period from 1981 to 1988 (Lewis and Grimes 1988). From this table, it is apparent that the selling price of corn varies considerably. For instance, the highest price for corn was in 1984 at a price of $164/dry tonne ($3.52/bushel). The lowest price was only 2 years later at a price of $56.80/dry tonne ($1.22/bushel). Co-product prices also varied considerably over this time frame. The highest co-product price for dry milling occurred in 1984 at a price of $76.90/dry tonne ($1.65/bushel) of corn processed. The low co-product price for dry milling was only a year later

Table 79. Extremes in corn and coproduct prices for dry- and wet-milling processes[1]

	Year	$/dry tonne of corn[2] ($/liter ethanol produced)		
		Corn Cost	Coproduct Price[3]	Net Cost[4]
High corn cost				
Dry milling	1984	164.00 (0.358)	69.40 (0.151)	94.60 (0.207)
Wet milling	1984	164.00 (0.372)	80.10 (0.182)	83.90 (0.190)
Low corn cost				
Dry milling	1986	56.80 (0.124)	48.90 (0.107)	7.90 (0.017)
Wet milling	1986	56.80 (0.129)	58.20 (0.132)	-1.40 (-0.003)
High co-product price				
Dry milling	1984	154.00 (0.336)	76.90 (0.168)	77.10 (0.168)
Wet milling	1983	158.00 (0.357)	86.70 (0.197)	71.30 (0.160)
Low co-product price				
Dry milling	1985	130.00 (0.284)	35.90 (0.078)	94.10 (0.206)
Wet milling	1985	116.00 (0.264)	57.80 (0.131)	58.20 (0.133)
High net cost				
Dry milling	1985	130.00 (0.284)	35.90 (0.078)	94.10 (0.206)
Wet milling	1984	149.00 (0.337)	62.00 (0.141)	87.00 (0.196)
Low net cost				
Dry milling	1986	56.80 (0.124)	48.90 (0.107)	7.90 (0.017)
Wet milling	1986	56.80 (0.129)	58.20 (0.132)	-1.40 (-0.003)

[1] Data from Lewis and Grimes (1988) without credit for sale of carbon dioxide for 1981 to 1988.

[2] Multiply values shown by 0.02151 to obtain price in $/bushel.

[3] Co-product price is revenue generated by co-product sales/tonne of corn processed.

[4] Net cost is defined as the cost of the corn less the revenue generated from the sales of co-products produced/dry tonne of corn.

at $35.90/dry tonne ($0.77/bushel). In the wet-milling operation, the highest price for co-products was in 1983 at $86.70/dry tonne ($1.86/bushel) of corn processed, while the lowest co-product price for wet milling was in 1985 at $57.80/tonne ($1.24/bushel). All of the values presented in table 6 do not include co-product revenue from carbon dioxide sales.

Perhaps a more telling indicator of the cost of corn to the ethanol producer, termed the net cost of corn is presented in table 79. The net cost of corn is defined as the cost of the corn purchased minus the selling price of the co-products. For dry milling, the highest net cost of corn was in 1985 at $94.10/tonne ($2.03/bushel) of dry corn, while the lowest net cost of corn was only one year later at $7.90/tonne ($0.17/bushel) of dry corn. In the wet milling, the highest net cost of corn was in 1984 at $87.00/tonne ($1.86/bushel) processed. Because of the number of co-products generated in wet milling and their fairly high value, the low net price of corn was actually a negative $1.40/tonne ($0.03/bushel) of dry corn in 1986—in effect, the processor was being "paid" to convert the corn into ethanol because of high co-product revenues.

Also shown in table 79 is the corn cost in terms of the volume of ethanol produced. The first column indicates the cost of corn only, while the second column, labeled co-product prices, provides the value of the co-products in terms of the volume of ethanol produced. The difference between these two entries is provided in the third column, net cost, in terms of the volume of ethanol produced. The highest net cost of corn corresponds to about $0.20/liter ($0.80/gallon) of ethanol. By comparison, ethanol is only worth about $0.30 to $0.35/liter ($1.15 to $1.35/gallon) of ethanol. On the other hand, the low net price of the corn feedstock is practically zero.

5.1.2 Corn Ethanol Economics. Table 80 presents the operating and capital costs associated with the production of ethanol from corn based on the USDA Cost Effectiveness Study (USDA 1987). These prices are all for a grass roots facility (a facility built on previously unutilized ground) and are translated into 1990 dollars using Nelson-Farrar cost indices (Oil and Gas Journal 1990). The values shown indicate lower capital costs for larger scale plants because of economies of scale. One would typically expect the capital costs associated with wet-milling operations to be at the high end of the values shown, while dry-milling operations would be at the lower end of the range. Also included in the table are the range of fuel and electricity costs expected, depending on the efficiency of the operation and to some extent the scale. Chemicals, enzymes, and yeast costs are greatly influenced by whether or not these ingredients are produced on site or are purchased. Maintenance and personnel costs along with insurance rates are included in the table as well.

It is important to note that lower capital costs are possible than those shown in table 80 for plants that are integrated into existing facilities. Such op-

Table 80. Variable, fixed, and capital costs for production of ethanol from corn[1]

	Plant size, ML/year (M gal/year)	
	<150 (40)	150–950 (40–250)
Capital Investment		
$/annual liter	0.87	$0.58–0.72
($/annual gallon)	(3.28)	(2.19–2.73)
Fuel, $/liter produced ($/gallon)		
Coal	0.029–0.040 (0.11–0.15)	0.029–0.040 (0.11–0.15)
Electricity, $/liter produced ($/gallon)	0.011–0.016 (0.04–0.06)	0.011–0.016 (0.04–0.06)
Chemicals, enzymes, yeasts, $/liter produced ($/gallon)	0.010-0.032 (0.04-0.12)	0.010–0.032 (0.04–0.12)
Maintenance, $/liter produced ($/gallon)	0.029–0.043 (0.11–0.16)	0.029–0.043 (0.11–0.16)
Personnel, $/liter produced ($/gallon)	0.048 (0.18)	0.017 (0.06)
Taxes & Insurance, % of capital	2.0%	2.0%

[1] From USDA reference (1987) for a modern plant built on an undeveloped site (grass roots plant); transformed to 1990 dollars.

Table 81. Predicted selling price of ethanol from corn based on the economic parameters in Table 82[1]

Process	Plant Size ML/yr EtOH[2]	Capital	Feed	O&M	Coproducts	Ethanol
		(1990$/L EtOH)				
Wet Mill with Low Net Corn Cost	378	0.158	0.129	0.145	0.133	0.299
Wet Mill with High Net Corn Cost	378	0.163	0.338	0.144	0.141	0.504
Dry Mill with Low Net Corn Cost	189	0.129	0.125	0.141	0.107	0.288
Dry Mill with High Net Corn Cost	189	0.133	0.286	0.142	0.079	0.482

[1] Ethanol yields are 440 liters/tonne of corn for a wet-mill process and 458 liters/tonne of corn for a dry-mill process.

[2] Pure 100% ethanol.

erations can cut the capital costs approximately in half. On the other hand, poorly engineered plants can be twice as costly as the values given. Of course, such facilities would be unlikely to be economical.

Table 81 presents the estimated costs of production of ethanol from corn based on the data given in tables 79 and 80. Estimates are provided for large, efficient wet- and dry-milling operations in this table. Scenarios are given for high net costs of corn for each type of facility as well as for low net costs of corn. All values are 1990 dollars. From these cost estimates, it can be seen that co-product revenue has a substantial impact on corn ethanol economic viability. All costs are estimated based on the economic parameters provided in table 82 (Chem Systems 1990).

5.2 Biomass Ethanol

Ethanol is not yet produced commercially from lignocellulosic biomass in the United States. Therefore, the economics of the technology must be estimated from available information on feedstock costs and conceptual process engineering studies.

5.2.1 Feedstock Costs. Several forms of wastes such as agricultural residues, MSW, and forestry residues could be used to produce ethanol. Large tipping fees of $100/tonne ($90/ton) and more are paid for disposal of MSW in some regions of the country. Therefore, it is possible that such feedstocks might be obtained at no cost or the processor may be actually paid to accept such materials, although costs will no doubt be incurred in feedstock preparation and handling. Forestry residues have been estimated to cost from $20 to $36/dry tonne ($18 to $33/ton). Agricultural residues could cost in the range of $24 to $49/dry tonne ($22 to $44/ton) (Wyman and Hinman, 1990, Lynd 1989).

Energy crops can also be used for production of ethanol from biomass. However, such technology has not been demonstrated, and estimation of the

Table 82. Economic parameters for estimating ethanol selling price for corn and lignocellulosic biomass[1]

U.S. dollars, fourth quarter 1990.

Operating rate of 91%, equal to 8,000 hours/year.

General plant overhead at 65% of operating costs.

Direct overhead at 45% of labor and supervision.

Maintenance at 3% of inside battery limits costs.

Insurance and property taxes at 1.5% of total fixed investment.

No sales expenses.

No inflation.

Working capital is paid out at plant startup and recovered at the end of the life of the project. It is calculated as the sum of the following:

> Feedstock inventory - 1 month's supply of raw materials valued at delivered prices.
>
> Finished product inventory - Half a month's supply of principal product and coproducts (if any) valued at the gross cost of production based on liquid or solid product storage and excluding items not normally stored.
>
> Accounts receivable - 1 month's gross cost of production.
>
> Cash - 1 week's out-of-pocket expenses estimated at the gross cost of production less depreciation.
>
> Less a fifth item:
>
> > Accounts payable - 1 month's supply of raw materials at delivered prices.

Capital charges[2] are calculated for a 10% discounted cash flow rate of return with the following parameters:

> Three years of construction with expenditures of 30% in the first year, 50% in the second year, and 20% in the third year.
>
> Fifteen years of operation.
>
> Income tax rate of 37%.
>
> Capacity buildup to 60% of nameplate capacity in the first year of operation, 80% in the second year, and 100% from the third year onward.
>
> Straight line depreciation over 5 years for inside battery limits and 15 years for outside battery limits investment.

[1] Based on Chem Systems 1990

[2] Addition of an annual capital charge calculated as 20% of the total capital investment to the cost of production will give approximately the same predicted selling price.

cost of these materials is somewhat more difficult. It is thought that woody crops could be produced at a cost of $34 to $68/dry tonne ($31 to $62/ton). Herbaceous crops are estimated to cost from $27 to $45/dry tonne ($24 to $41/ton) (Wyman and Hinman, 1990).

5.2.2 Biomass Ethanol Economics. The economics of ethanol production from lignocellulosic biomass have been the subject of a number of investigations over the past 10 years (Chem Systems 1984; Arthur D. Little 1984; Badger Engineers 1984; Stone and Webster 1985a and 1985b). Processes have been studied for both acid- and enzyme-catalyzed breakdown of cellulose to form glucose sugar followed by fermentation of the glucose to ethanol. These studies have also included conversion of hemicellulosic sugars into products such as furfural and other chemicals as well as ethanol. Through these studies, enzymatic conversion based on SSF technology is favored to be competitive in the near term while offering substantial opportunities for improvement. Recently, Chem Systems performed a study for the National Renewable Energy Laboratory (NREL) through the support of the U.S. Department of Energy, to estimate the cost of ethanol from lignocellulosic biomass (Chem Systems 1990). The Chem Systems analysis was based on dilute acid pretreatment of biomass to break down the hemicellulose fraction to release xylose and other sugars into solution. A small fraction of the wet solids from pretreatment, containing primarily cellulose and lignin, was sent

Table 83. Capital and operating cost estimates for ethanol production from lignocellulosic biomass

	Reference Case[1]	Larger Scale[1]	Modified Case[2]
Plant Size			
Feed Rate, dry tonnes/day	1742	8078	1742
Product Rate, ML/year (denatured, hydrous)	219	1096	221
Feed Price, 1990 US $/dry tonne	46	46	46
Capital Cost, MM US $ (1990)			
Feed Handling	7.13	28.27	7.16
Prehydrolysis	23.23	91.84	23.68
Xylose Fermentation	6.21	24.66	6.16
Cellulase Production	2.68	10.64	2.76
SSF Fermentation	22.26	88.41	20.93
Ethanol Purification	3.88	10.98	3.99
Offsite Tankage	3.14	7.58	4.09
Environmental Systems	4.10	11.71	3.96
Utilities/Auxiliaries	59.36	169.46	55.66
Erected Plant Cost	131.98	443.55	128.39
Start-up	6.56	22.16	6.42
Total Capital Investment	138.53	465.71	134.81
Working Capital	6.63	29.94	6.31
Operating Costs, MM US $/Year (1990)			
Variable Costs			
Feedstock	26.88	134.39	26.88
Catalyst and Chemicals	9.38	46.88	8.14
Solids Disposal	0.40	2.00	0.40
Water	0.12	0.58	0.14
Utilities	(3.22)	(16.10)	(4.15)
Fixed Costs			
Labor	1.68	3.34	1.57
Maintenance	4.16	13.86	3.85
General Overhead	3.79	11.18	3.52
Direct Overhead	0.75	1.50	0.71
Insurance, Property Tax	2.08	6.99	2.02
Total Operating Cost	46.01	204.61	43.08

[1] Chem Systems 1990
[2] Hinman et al. 1992

to an enzyme production step where cellulase enzymes were produced by the fungus T. reesei. The enzymes were then added to the bulk of the pretreated solid material along with yeast for conversion into ethanol by the SSF process. In this economic study, the xylose and other sugars released during pretreatment were converted into ethanol based on data for the genetically engineered E.coli strain developed at the University of Florida. Continuous fermentation was assumed for all fermentation steps other than enzyme production, which was a batch operation. The ethanol produced during the fermentation operations was recovered by a conventional distillation system. Gasoline was added to denature the ethanol for sale as a neat fuel. The resulting fuel contained about 90.3% ethanol, 4.7% water, and 5% gasoline by weight. The lignin recovered from the bottom of the distillation column was burned as a boiler fuel to provide all the heat and electricity for the process as well as excess electricity that was sold for additional revenue. Chem Systems estimated the capital and operating costs for the process and from that, estimated the selling price of ethanol.

Table 83 provides the capital and operating costs for ethanol production from lignocellulosic biomass, as estimated by Chem Systems. The price estimates were translated from the 1987 dollars used in the Chem System study to 1990 dollars in table 83 based on the Nelson-Farrar Cost Index (Oil and Gas Journal 1990). Costs were derived at biomass feed rates of 1,742 and 8,708 dry tonnes/day (1,920 and 9,600 tons/day). Feedstock was assumed to cost $46/dry tonne ($42/ton). At the

Table 84. Discounted cash flow for ethanol production from lignocellulosic biomass for the Chem Systems Reference Case (all dollars in millions)

Capital Cost	$131.98
Start-up Costs	$6.56
Total Plant Cost	$138.53
Ethanol Selling Price	$0.345/Liter
Production Rate	219 Million Liters/Year

Items	Years																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Percent of Capital Paid	30.0%	50.0%	20.0%															
Capital Invested	$39.59	$65.99	$26.40															
Start-up Costs				$6.56														
Working Capital				$6.63														$(6.63)
Total Annual Capital Outlay	$39.59	$65.99	$26.40	$13.19	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$(6.63)
Total Capital Investment	$39.59	$105.58	$131.98	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$145.16	$138.53
Percent of Nameplate	0%	0%	0%	60%	80%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Production Rate, MM Liters/Year				131.5	175.4	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2	219.2
Ethanol Revenue				$45.40	$60.53	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66	$75.66
Electricity Revenue				1.93	2.58	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22	3.22
Feedstock Cost				16.13	21.50	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88
Chemicals, Solids Disposal, Water				5.94	7.92	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90	9.90
Fixed Operating Costs				12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45	12.45
Total Costs				$34.52	$41.88	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23	$49.23
Income Before Depreciation, Taxes				$12.81	$21.23	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65	$29.65
Depreciation				17.52	17.52	17.52	17.52	17.52	4.44	4.44	4.44	4.44	4.44	4.44	4.44	4.44	4.44	4.44
Income After Depreciation				$(4.71)	$3.72	$12.14	$12.14	$12.14	$25.21	$25.21	$25.21	$25.21	$25.21	$25.21	$25.21	$25.21	$25.21	$25.21
Income Tax				0.00	1.37	4.49	4.49	4.49	9.33	9.33	9.33	9.33	9.33	9.33	9.33	9.33	9.33	9.33
Income After Tax				$(4.71)	$2.34	$7.65	$7.65	$7.65	$15.88	$15.88	$15.88	$15.88	$15.88	$15.88	$15.88	$15.88	$15.88	$15.88
Total Cash (Depreciation plus Income After Tax)				$12.81	$19.86	$25.16	$25.16	$25.16	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32
Annual Cash Flow	$(39.59)	$(65.99)	$(26.40)	$(0.38)	$19.86	$25.16	$25.16	$25.16	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$20.32	$26.95
Discounted Cash Flow	$(39.59)	$(59.99)	$(21.81)	$(0.28)	$13.56	$15.62	$14.20	$12.91	$9.48	$8.62	$7.84	$7.12	$6.48	$5.89	$5.35	$4.87	$4.42	$5.33
Cumulative Discounted Cash Flow	$(39.59)	$(99.58)	$(121.40)	$(121.68)	$(108.12)	$(92.49)	$(78.29)	$(65.38)	$(55.90)	$(47.28)	$(39.44)	$(32.32)	$(25.84)	$(19.96)	$(14.60)	$(9.74)	$(5.31)	$0.02

lower feed rate, 219 million liters/year (58 million gallons/year) of denatured ethanol could be produced, while at the higher feed rate 1,096 million liters/year (290 million gallons/year) of denatured ethanol could be derived. The total capital investment required, including start-up costs, are about $139 million for the smaller plant size and $466 million for the larger scale operation. Total operating costs for the smaller scale plant are estimated to be about $46 million, while those for the larger scale plant are estimated to be about $205 million.

Table 84 presents a discounted cash flow analysis for the smaller scale case studied by Chem Systems. This analysis takes into account start-up costs as well as working capital requirements for the plant and is based on financial parameters provided in table 82. Based on this discounted cash flow analysis, an ethanol selling price of $0.345/liter ($1.31/gallon) of denatured fuel is projected for this Chem Systems reference case when converted to 1990 dollars. This selling price covers all costs of production plus provides a 10% real rate of return on the investment as outlined previously. A similar analysis, as summarized in table 85, predicts an ethanol selling price of about $0.278/liter ($1.05/gallon) for the larger scale Chem Systems process. The later price is somewhat below the current market price of ethanol of about $0.30 to $0.35/liter ($1.15 to $1.35/gallon).

Based on the Chem Systems study, NREL investigated several options to further reduce the price of ethanol from lignocellulosic biomass (Hinman et al. 1992), and a process design was developed with costs summarized in table 83. A lignocellulosic biomass feed rate of 1,742 dry tonnes/day (1,920 tons/day) was assumed with a denatured hydrous ethanol production rate of 221 million liters/year (58 million gallons/year). Once again, the feedstock price was taken as $46/dry tonne ($42/ton) in 1990 dollars. Capital and operating costs were estimated as shown for this process and the results used in a cash flow analysis to predict the selling price of ethanol. In this case, an ethanol selling price of about $0.324/liter ($1.23/gallon) was predicted for the smaller scale plant, as shown in table 85. Even though this price is somewhat higher than that predicted by Chem Systems for a larger scale operation, it shows that ethanol could be produced from lignocellulosic biomass at the smaller scale at prices competitive with ethanol from corn. Furthermore, immediate opportunities have been identified to reduce the costs of ethanol somewhat further by optimizing enzyme loading in combination with SSF performance.

Table 85. Cost projections for production of ethanol from lignocellulosic biomass

Process	Plant Size[a] ML/yr EtOH	Capital	Feed	O&M	Electricity	Ethanol
		(1990$/L EtOH)				
Reference	219	0.135	0.123	0.102	0.015	0.345
Larger Scale	1,096	0.091	0.123	0.079	0.015	0.278
Modified	221	0.130	0.121	0.092	0.019	0.324

[1] Denatured, hydrous ethanol

5.2.3 Opportunities for Advancement. Based on the cash flow analysis presented, enzymatic conversion of lignocellulosic biomass using technology available in 1982 would have resulted in an ethanol selling price of about $0.98 (1990 dollars) per liter ($3.70/gallon) (Wright 1988a and 1988b). Through advancements in this technology, the price has been reduced to about $0.32 per liter ($1.23/gallon) now (Hinman et al. 1992). Furthermore, a substantial number of opportunities have been identified to reduce the price to $0.17 to $0.18 per liter ($0.67/gallon). These include improving the yields of ethanol through the development of better enzymes that can be produced at lower costs. Enzymes that can provide faster breakdown of cellulose could reduce conversion time from about 5 to 7 days to only 2 to 3 days and result in significant reduction in capital and operating costs. More efficient pretreatment systems can result in enhanced yields of ethanol during the enzymatic hydrolysis step, through greater accessibility of the cellulose, as well as less degradation of cellulose, xylose, and other carbohydrates during the pretreatment step. Improvements in pretreatment technology could also result in lower capital and operating costs. Improved organisms to enhance yields of ethanol from the hemicellulose sugars could be developed, along with lower costs media, for each of the fermentation operations. The economics would benefit from increased ethanol concentrations of around 6% to 8%, although advanced distillation systems may make recovery of lower ethanol concentrations cost effective. Production of co-products from the lignin fraction, other than electricity, could also improve the economics of ethanol production. Because feedstock costs are a significant fraction of the final product selling price, improvements in feedstock related technology could improve the economics of ethanol production through greater economies of scale, decreased feedstocks costs, and less feedstock that cannot be fermented into ethanol. The number of mutually exclusive paths for reducing the cost of ethanol production from lignocellulosic biomass is so substantial that the probability of achieving the target price of about $0.17 to $0.18/liter ($0.67/gallon) is quite high.

6. Strengths

Ethanol has immediate application for blending with gasoline. Through the implementation of the Clean Air Act Amendments of 1990, the need for oxygenates such as ethanol and ETBE is expanding dramatically. In addition, as the technology for production of ethanol from lignocellulosic biomass is improved, the cost of ethanol can be reduced, and the market could grow further. Low cost feedstocks are immediately available that will allow early introduction of this technology into the oxygenate market. As the opportunities to lower the cost of ethanol are realized, the price could drop enough to make neat fuel use viable.

6.1 Ethanol's Flexibility as a Fuel

Ethanol can be directly blended with gasoline. In this application, ethanol is valued as a fuel extender, octane booster, and an oxygenate. Combining the merits of each of these attributes with the existing tax incentive to promote the use of ethanol produced from biomass results in an immediate competitive position at projected selling prices for lignocellulosic biomass.

Ethanol can also be converted into ETBE for blending with gasoline. ETBE is valued as a fuel extender, octane booster, and oxygenate. At slightly below existing corn ethanol process, ethanol would see wide use for ETBE production because of the ability of ETBE to reduce the vapor pressure of gasoline.

Finally, ethanol can be used as a virtually pure or neat fuel. Because ethanol has a low vapor pressure and high octane along with other favorable fuel properties, it is one of the front running options for replacement of gasoline to address air pollution issues. Its price has been historically too high to compete with other options such as methanol, but if opportunities can be realized to reduce the price to be competitive with gasoline, ethanol could see widespread use as a neat fuel.

6.2 Opportunities for Technology Improvement

Technology for production of ethanol from lignocellulosic biomass is rapidly evolving, and the power of modern biotechnology and bioprocessing can be called on to radically alter the economics. Because so many options are available for advancing the technology, the probability of success is quite high. Although some time will be required before the advances are realized and are shown to be commercially viable, the opportunity is promising to produce ethanol at a far lower cost in the future. Thus, those that enter the marketplace for ethanol production from lignocellulosic biomass now can look forward to technology that could result in lower costs and expanded markets in the future. Furthermore, pilot plants are being constructed at the National Renewable Energy Laboratory (NREL) and other sites to demonstrate the technology for ethanol production from lignocellulosic biomass. These pilot plants will demonstrate the viability of technology that is available now as well as provide a facility to develop and test improvements in the technology in the future. Such facilities could provide significant support to those that commercialize lignocellulosic conversion technology in the near term.

6.3 Near-Term Availability of Feedstocks

A diverse range of existing lignocellulosic materials can be converted into ethanol, including waste materials such as MSW, agricultural residues, and forestry wastes. Many of these wastes may be available at low costs, which makes them attractive for early introduction into the marketplace. Another potential source of low-cost feedstocks in the near term is cellulose fines from the paper and pulp industry. Additionally, the low-value fiber in corn that is now blended with corn gluten feed in the wet-milling industry is high in cellulose and hemicellulose content. In the dry milling of corn, the fiber is left behind in the DDGS co-product that is sold as animal feed. Conversion of the fiber from either one of these animal feed co-products into ethanol could enhance overall ethanol yields from the plant by about 14% to 16% and result in a higher protein content in the animal feed co-products that may have a higher market value. The latter could be true because animal feed co-products are generally sold on the basis of their protein content, and conversion of the fiber into ethanol would leave a higher fraction of protein.

Many other lignocellulosic materials are also now available that could serve as very low-cost feedstocks for early introduction of this technology in the marketplace. Although the quantity of low-cost materials is limited as far as substantial impact of ethanol on the transportation fuel market, such feedstocks are still sufficient to provide an opportunity for early introduction of ethanol technology at a significant scale, as evident by table 76. Then, as advances are made in the technology for ethanol production from lignocellulosic biomass, higher cost energy crops could be employed as feedstocks for ethanol production at prices competitive with conventional fuels.

7. Weaknesses/Barriers

If entering the ethanol business, it is important to ensure the issues impacting the markets, the technology, and the source of raw material are considered. Some controversies surround the use of ethanol as a fuel, and the entrepreneur must be aware of these before embarking in this field. In addition, it is important to establish a sound technology position and recognize opportunities to reduce the risk in the future. Finally, a sufficient source of feedstock must be available.

7.1 Fuel Issues

Although ethanol increases octane and provides oxygen when blended with gasoline, it is not as widely used as one might expect based on the value calculated for the product. This contradiction may be partly due to some perceived difficulties with ethanol blends. First, ethanol is not fungible with gasoline; that is, it is not completely compatible, and problems such as separation in water can result with the storage and transport of ethanol in pipelines. Of particular concern is the tendency of ethanol to phase separate with any water present in pipelines or storage tanks (Ludlow 1989). In addition, the vaporization characteristics of ethanol blends are different than those of regular gasoline. For instance, blending ethanol with gasoline increases the Reid vapor pressure (RVP) by about 3.4 to 6.9 kilopascals (05. to 1.0 psi). As a result, ethanol blends are more subject to vapor lock in engine fuel lines. Although the characteristics of the base gasoline could be changed to accommodate ethanol, ethanol is primarily blended with regular gasoline by small blenders who are not equipped to change the base-blending stock to compensate for ethanol addition. As a result, some of the public perceive ethanol unfavorably and are reluctant to purchase fuels that contain ethanol. Thus, it may be necessary to sell ethanol at a somewhat lower price than one might expect based on its fuel properties to compensate for the poor public perception. The fact that most major gasoline producers do not manufacture ethanol may lead to lower use as well.

One of the critical issues currently facing ethanol use in blends is the impact of the increase in RVP on air quality. Greater evaporative emissions result with increased RVP, and more of the fuel mixture is released into the atmosphere during vehicle refueling and as running losses when the fuel moves through the fuel system. Thus, even though use of ethanol has been shown to reduce the emissions of unburned hydrocarbons and carbon monoxide from the tailpipe of vehicles, many argue that the higher evaporative and running loss emissions more than compensate for this benefit (Anderson 1992a and 1992b). Release of unburned hydrocarbons from fueling and running losses, as well as carbon monoxide and other tailpipe emissions, contributes to the formation of ozone in cities such as Los Angeles. As a result there is still considerable debate about whether or not direct ethanol blends should be allowed during summer months under the Clean Air Act Amendments to improve urban air quality. The decision on the viability of ethanol in this market will have a substantial impact on its future sales. On the other hand, because ETBE lowers the RVP of gasoline mixtures, these factors are not an issue. Pure ethanol also has a very low vapor pressure and would have advantages in addressing these emissions.

7.2 Intellectual Property

An important aspect of commercializing ethanol technology could be development of protected technical positions through patents and trade secrets. As one brings this technology into the marketplace successfully, other companies may wish to follow with similar processes. If the technology is not properly protected, these companies will be free to utilize the success of the first risk-takers to their advantage. However, if these first companies into the market have proper protection for their technology, they can prevent others from capitalizing on their success without proper remuneration.

Another aspect to intellectual property considerations is that some of the key technologies for ethanol production are already owned by companies in this business. For instance, strains of E.coli, Kliebsella oxytoca, and other microorganisms have been genetically engineered to ferment xylose and other five-carbon sugars to ethanol, with apparently high yields. Because these technologies are protected, others cannot apply them without proper licensing arrangements with the owners of the inventions. Similar considerations apply to other technologies in the production of ethanol from biomass. Thus, if companies wish to produce ethanol from lignocellulosic biomass, they should be thoroughly familiar with the technologies available and ownership positions in these technologies before embarking on this venture.

7.3 Technology Maturity

The technology for production of ethanol from lignocellulosic biomass has emerged rapidly over the last few years. However, despite the favorable cost projections for ethanol production and the opportunity for significant further advancements, the technology has mainly been tested at the bench scale. A critical need is to establish the performance of the technology in fully integrated systems. Furthermore, integrations of this type must be carried to a large enough scale so that meaningful mechanical, biological, and chemical performance data can be gathered. It is necessary to establish how the various chemicals that result from each process step and accumulate through recycling of water affect process performance, particularly for biologically catalyzed steps. Furthermore, good data are needed on energy requirements for mixing and other mechanical operations in the process. Pilot plants are being constructed at NREL and other locations to gather such data, which will enhance the prospects for technology commercialization. However, until those data are available, considerable uncertainty exists about how well the processes will perform versus the projections made in process economics studies.

7.4 Feedstock Supply

One of the critical issues facing ethanol production from lignocellulosic biomass is ensuring an adequate supply of feedstock for a very large-scale plant. Before building a large plant, a guaranteed supply of feedstock is needed at an established price. However, no one is willing to plant a large land area with feedstock without having a guaranteed user of that material. Because woody forms of biomass can require five to ten years to establish growth, it may be difficult to get large-scale biomass systems in place that will feed a commercial plant when it is ready to operate. Furthermore, the establishment of such a large biomass supply entails substantial investment in addition to that associated with building the plant for ethanol production. The result is that the combined capital requirements for construction of a plant plus developing a reliable source of biomass may be too great for many start up companies to undertake. Use of waste materials such as municipal solid wastes or agricultural and forestry wastes which could be contracted for on a long-term basis could alleviate this difficulty for initial plants until the technology is established. Herbaceous crops can also be established in only a year to provide a source of energy crops more quickly for ethanol production.

8. Opportunities

Demand for alternative fuels and oxygenates such as ethanol in the United States has grown steadily over the last few years and is expected to skyrocket in the next two decades and beyond. Several factors including energy security, economic prosperity, and environmental concerns are responsible for this increased demand.

8.1 Regulatory Requirements for Oxygenates

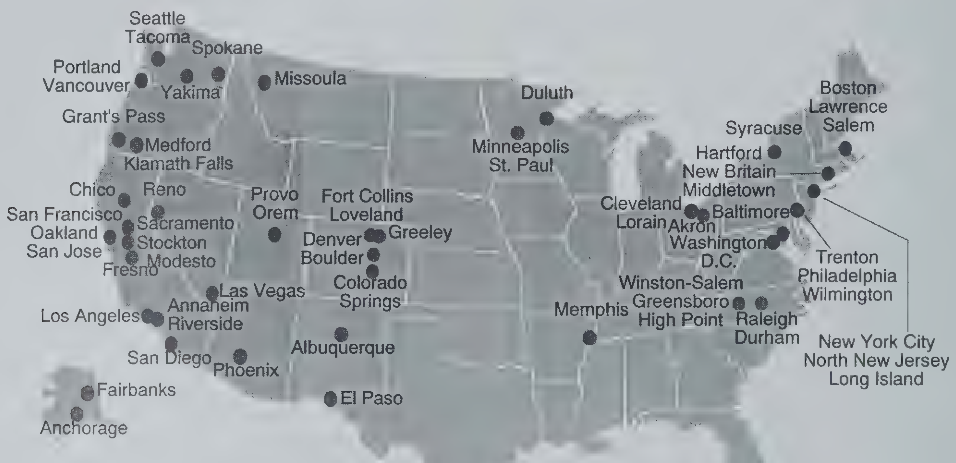
Conventional transportation fuels have significant adverse impacts on land, air, and water resources. Air pollution, global climate change, oil spills, and toxic waste generation can result from the use and production of petroleum-based transportation fuels. Air pollution from transportation fuels occurs during transfer and storage as well as end use. Reactive hydrocarbons and toxic compounds such as 1,3 butadiene and benzene are the principal air emissions resulting from fuel storage and transfer. Combustion products include carbon dioxide, carbon monoxide, nitrogen oxides (NO_x), reactive hydrocarbons, and small amounts of particulate matter and sulfur dioxide.

Much of the air pollution in the United States is caused by petroleum-based transportation fuels. Sulfur dioxide, particulate matter, carbon monoxide, nitrogen oxides, and ozone formed from reactive hydrocarbons and nitrogen oxide in the presence of sunlight are pollutants, and their emissions are regulated. Each of these pollutants has serious adverse impacts on human health and the environment, and the Clean Air Act and its Amendments of 1990 are directed at regulating releases that contribute to their accumulation. Ozone causes respiratory damage in humans and may also adversely affect crops (U.S. Congress 1990). Oxides of nitrogen and sulfur combine with water vapor in the atmosphere to form acid rain. In addition, nitrogen oxide (NO_2) can cause fatal lung damage and nitric oxide (NO) is an asphyxiant (Danielson 1973). Carbon monoxide also results in health risks at concentrations exceeding 9 parts per million (ppm). Sulfur dioxide and particulate matter reduce visibility and have a synergistic effect as lung and eye irritants. The California Air Resources Board (CARB) estimates that 43% of reactive organic gases, 57% of the nitrogen oxides, and 82% of carbon monoxide in the major California urban areas resulted from automobile emissions (Sperling 1990). Air pollution has enormous economic, social, and environmental impacts including human sickness and death, agricultural productivity decreases, building corrosion, visibility reduction, and wildlife habitation (De Luchi et al. 1987). For example, use of gasoline and diesel fuel increases deaths by 30,000 in the United States annually. The external non-market cost of air pollution in the United States is estimated to range from $11 billion to $187 billion annually (Sperling 1990). If these costs were factored into the price of gasoline, alternative fuels might have been introduced into the U.S. market much sooner.

Thirty-nine areas in the United States exceed the National Ambient Air Quality Standards (NAAQS) for carbon monoxide (Federal Register

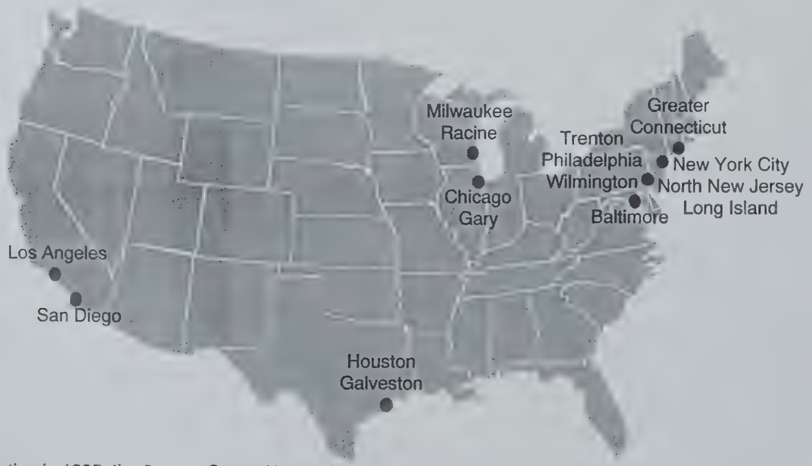
1992). Through the Clean Air Act Amendments of 1990, these areas must use fuels with a minimum oxygen content of 2.7% for at least 4 winter months beginning on November 1, 1992. For those areas that still do not attain the standards by December 2000, the minimum oxygen content for fuels will be raised to 3.1% (Scherr et al. 1991). These oxygenated gasoline requirements will affect 32.1% of the gasoline pool. In 1989, this would affect a gasoline demand of almost 140 gigaliters (37 billion gallons). Figures 64 and 65 show the areas of the United States currently subject to these provisions of the Clean Air Act Amendments of 1990 for carbon monoxide and ozone, respectively.

Some states and air quality regions may have different requirements from those listed above. CARB has petitioned the EPA to lower the oxygen content of its winter time blends from the minimum 2.7% required to a range of 1.8%–2.2% (Octane Week 1991). Although emissions of carbon monoxide increase with lower fuel oxygen content, emissions of NO_x decrease. Because of California's severe ozone non-attainment status, CARB believes that NO_x is a bigger problem than carbon monoxide and that this trade-off is warranted. Several other sources support this position and have indicated that the EPA has been remiss in aggressively reducing emissions of volatile organic com-



- As of February 1992, 39 areas are required to sell oxygenated gasoline.
- In 1993, an estimated 12-14 billion gallons of gasoline will be governed by the Clean Air Act provisions.

Fig. 64. 1990 Clean Air Act Amendments—Carbon Monoxide Nonattainment Areas.



- Starting in 1995, the 9 worst Ozone Nonattainment Areas in the country must sell only reformulated gasoline.
- Collectively, these areas account for approximately 25% of the motor fuel sold in the country.

Fig. 65. 1990 Clean Air Act Amendments—Ozone Nonattainment Areas.

pounds (VOC's) as a precursor to ozone and ignoring NO_x, another precursor to ozone (Octane Week 1991a). Some studies have shown that NO_x has a much bigger role to play in ozone formation than VOC's, depending on the relative amounts of these two components in the air.

In other regions, the carbon monoxide control season may be longer than the 4-month minimum required by the Clean Air Act Amendments because of the severity and the duration of the elevated levels of carbon monoxide in these areas. The EPA has proposed increasing carbon monoxide seasons in 6 areas: New York City, Northern New Jersey, Las Vegas, Phoenix, Los Angeles, and Spokane (Federal Register 1992). However, New York City has made a counter proposal of a 2.7% oxygen content for 5 months and a 2.0% oxygen content for the remaining 7 months.

Beginning in 1995, nine areas with ozone concentrations of greater than 0.16 ppm and a population of greater than 250,000 will be required to use reformulated gasoline (RFG). RFG must contain at least 2% oxygen by weight, no more than 25% by volume aromatics, less than 1% by volume benzene, and no lead or other heavy metals. RFG must also contain detergents to prevent the accumulations of deposits in engines or fuel supply systems.

Vehicles using RFG must meet several other performance-based emissions standards. Aggregate emissions of ozone-forming VOC's and toxics (e.g., benzene, 1,3 butadiene, polycyclic organic matter, acetaldehyde, and formaldehyde) must be 15% below (on a mass basis) the same emissions from vehicles using "baseline gasoline." In addition, emissions of NO_x from baseline vehicles using RFG must not be greater than the NO_x emissions from baseline vehicles using "baseline gasoline." In 2000, the required reduction in both VOCs and toxics increases to 25%. If the EPA decides this level is technologically or economically infeasible, however, the required decrease can be reduced to 20%.

Reformulated gasoline standards have not yet been finalized, but EPA has issued its proposed rule based on the accord developed by the Clean Fuels Advisory Committee during its regulatory negotiations (Reg-Neg) in August 1991. Twenty-eight representatives signed the accord from a diverse group of industries such as alternative fuels, petroleum refining, auto manufacturing, and agriculture. State regulatory agencies and the EPA also signed the accord. This process, outlined in the Clean Air Act Amendments of 1990, is designed to avoid the lengthy court battles that usually follow a ruling.

The nine affected areas represent 22% of the U.S. gasoline demand (Jones and Lareau 1991). If all potential ozone non-attainment areas opt into the program, almost 54% of the U.S. gasoline supply would require reformulation. Some overlap with the oxygenate program exists. About 26% of all U.S. gasoline is supplied to areas that are affected by the oxygenate and reformulated gasoline requirements (Jones and Lareau 1991).

In addition to the federal regulations, aggressive air pollution policies are being implemented in the state of California as well as individual air quality control regions comprised of large metropolitan areas such as Los Angeles. These regulations will also affect the markets for both oxygenates and alternative fuels and are likely a good indication of the direction of future regulations.

The potential for ethanol as a direct blending agent or use of ETBE is substantial in the United States. Currently, about 3.8 billion liters/year (1.0 billion gallons/year) of ethanol produced from corn is blended with gasoline. This level is somewhat less than 1% of the gasoline market. With mandates under the Clean Air Act Amendments of 1990 for enhanced oxygen levels in gasoline in cities occupied by more than half the U.S. population, the growth in the oxygenate market in the near future will be substantial. When ethanol is produced at prices competitive with MTBE, it would gather a substantial fraction of that market. Blending oxygenates in half of the gasoline in the United States could evolve into an annual market on the order of 19 billion liters (5.0 billion gallons) of ethanol. Even if ethanol shared this market equally with MTBE, on the order of 9 to 10 billion liters (2.4 to 2.6 billion gallons) of ethanol could be required annually within the next several years.

8.2 Neat Fuel Needs

Domestic transportation fuels are almost exclusively (about 97%) derived from petroleum and account for about 64% of the total petroleum used in the United States. Greater than one-fourth of the total U.S. energy use is consumed directly by the transportation sector, and when indirect energy uses (e.g., road building and repair, petroleum refining) are included, energy consumption in this sector rises to 40% (Gordon 1991).

Few substitutes are currently available for petroleum-based transportation fuels, and the mobility of the United States is extremely vulnerable both strategically and economically to supply disruptions. Iraq's invasion of Kuwait as well as the energy crisis of the 1970s underscore this vulnerability. For example, the estimated cumulative economic impact of the 1973–74 embargo and the 1979 petroleum cutoff was a gross national product (GNP) loss of at least 10% (100 billion dollars) in 1985. Petroleum imports also have a major impact on the trade deficit; in 1989 oil imports contributed about 40% ($44.7 billion of $111 billion) of the trade deficit.

The federal Alternative Motor Fuels Act (AMFA) of 1988 affects the neat ethanol market. It promotes the use of alternative fuels, including ethanol, in government fleet vehicles as the first step in their large-scale commercialization. The federal government and many state governments are providing incentives for the production of ethanol from renewable resources. The market for ethanol could eventually expand to up to 530 billion liters (140 billion gallons) as a neat fuel, provided it could be sold at prices competitive with gasoline and other substitute fuels that could enter the market.

In October of 1992, the 102nd Congress passed, and the President signed the first comprehensive energy policy act for this nation in 20 years. The Energy Policy Act, or EPACT, has many provisions which address multiple forms of energy production and use. Section 1202 characterizes the general goals of the Alcohol from Biomass Program which "shall be to advance the research and development to a point where alcohol from biomass technology is cost-competitive with conventional hydrocarbon transportation fuels, and to promote the integration of this technology into the transportation fuel section of the economy." It sets some specific goals for ethanol from biomass including: reduction of the cost of alcohol to 70 cents per gallon, improvement of the overall biomass carbohydrate conversion efficiency to 91 percent, reduction of the capital cost component of the cost of alcohol to 23 cents per gallon, and reduction of the operating and maintenance component of the cost of alcohol to 47 cents per gallon.

8.3 Niche Markets

Although substantial reductions in the price of ethanol from lignocellulosic biomass are possible through advances in the technology, ethanol from lignocellulosic materials can be produced at prices competitive with corn ethanol in the near term. Furthermore, examination of the costs summarized in table 85 reveals several areas for cost reduction. First, we see that feedstock costs comprise about $0.12/liter ($0.45/gallon) of the total projected ethanol price of $0.32/liter ($1.23/gallon). Therefore, if low-cost wastes such as MSW, agricultural or forestry residues, or other materials with little to no cost were utilized, a substantial reduction in price would be possible.

The return on capital comprises an element in the predicted selling price about equal to that of feedstock costs, on the order of $0.13/liter ($0.49/gallon) of ethanol produced. If low-cost debt that is tax deductible, such as municipal bonds, were used to finance the plant, these funds would leverage the investment and reduce the required ethanol selling price. Thus, arrangements with municipalities or utilities could provide valuable sources of financing for initial ethanol plants. Although leveraging is beneficial during good economic times, it must be remembered that it becomes detrimental if prices are squeezed.

The cost projections shown for ethanol production from lignocellulosic biomass are all based on construction of a grass roots plant. However, if an ethanol production facility were built at an existing chemical or fuel production site, many of these costs could be substantially reduced. It can be seen in the capital cost summaries in table 83 that utilities, environmental systems, and off-site tankage represent close to half the estimated total erected plant cost for an ethanol production facility. Therefore, if these costs could be reduced by using such systems in an existing plant, the price of ethanol could be reduced substantially.

In addition to these various steps to reduce costs, it may be possible to enhance co-product revenues from the ethanol process. For example, sale of electricity at a higher price than that assumed here could enhance revenues substantially. Alternatively, it may be possible to use better heat integration to increase the amount of electricity available for sale. If it were desirable to burn coal or other fuels in initial plants to provide steam and electricity, the lignin fraction of the biomass could be converted into higher value products, such as adhesives or other chemicals. Obviously, the revenue derived from the sale of more electricity or lignin co-products must be sufficient to cover the additional cost associated with generation of such products and provide greater net income.

8.4 Long-Term Benefits

Conventional transportation fuels contribute to the buildup of carbon dioxide and other gases in the atmosphere, which may trap heat and affect global climate change. The increase of greenhouse gases in the atmosphere is significant; for example, the level of carbon dioxide has risen by 25% since the mid 1800s and the concentration of methane is increasing at a rate 400 times the natural variability. Although the severity of the "greenhouse effect" is under debate, its possible consequences include the transformation of large areas of the world from heavily forested woodlands to deserts, loss of much of the corn belt in the Midwest, and flooding of coastal cities.

Carbon monoxide, although not a greenhouse gas itself, does increase atmospheric concentrations of methane and ozone and promotes reaction of NO to NO_2, the first step in ozone formation. It also reacts with the hydroxyl radical (OH), a scavenger of methane. Thus, carbon monoxide indirectly contributes to the buildup of greenhouse gases. In fact, the depletion of hydroxyl radicals is estimated to have an effect equivalent to the emissions of a few million tons of methane per year. The primary source of carbon monoxide emissions is transportation; about two-thirds of the U.S. carbon monoxide emissions result from transportation activities.

Production and use of petroleum-based transportation fuels also impart significant adverse effects to land and water resources as a result of oil spills and toxic waste generation. On the other hand, many alternative fuels could be made from the waste products of industries such as agriculture, pulp and paper, and food processing. Production of alternative fuels from these resources would have several benefits: it would lessen the environmental impact of these industries on land and water resources and would reduce their associated direct and indirect costs. In addition, another source of revenue for these industries would be created.

Use of surplus agricultural products and the development of the domestic energy crop industry are two other potential benefits for the production of alternative fuels, such as ethanol from biomass. Conversion of surplus agricultural products into alternative fuels utilizes products that would otherwise be allowed to decay, often releasing methane, a powerful greenhouse gas. It also generates additional revenue for farmers. Significant quantities of ethanol could be produced from this source. Substantial potential also exists for the creation of an energy crop industry.

9. Threats/Competition

Several octane boosters and oxygenates are commercially available for blending with gasoline other than ethanol. In addition, methanol is a strong candidate as a neat fuel to replace gasoline. In order to be successful, ethanol must not only compete with these alternates based on price, but environmental regulations can also influence the selection of oxygenates or neat fuels in the future.

9.1 Market Competition

The demand for oxygenates will increase significantly in the coming years. Most of these increases will occur before 1999 as the oxygenate and RFG standards are implemented. Initially, the market for ethanol will be as an oxygenate additive to gasoline in areas that do not meet air quality standards. A number of other oxygenates, including methyl tertiary butyl ether, tertiary amyl methyl ether, methanol, tertiary butyl alcohol, and isopropanol, will be competing for a share of this market. The demand for neat alternative fuels will also increase; however, it is not anticipated that this demand will be as rapid in the near-term as for oxygenates.

9.1.1 Methyl Tertiary Butyl Ether (MTBE). Alcohols are not fungible with gasoline—they do not ship and handle like other gasoline components. Therefore, they cannot be handled like conventional gasoline in common pipelines and tanks and are not swapped like normal gasoline. This drawback can be overcome if alcohols are converted to fungible ether blend stocks. Methanol can be reacted with isobutylene to form MTBE, which is currently the most popular oxygenate and is traded globally. Worldwide capacity today is approximately 257,700 barrels/day (132,000 barrels/day ethanol equivalent), and most of this is in the United States (Haigwood 1991). Use of MTBE outside of the United States is expected to rise as an oxygenate and with the global phaseout of lead compounds from gasoline. Currently, Europe is the only significant MTBE market outside the United States; however, the market in the Far East is expected to grow in the 1990s. This demand could be quite significant since Japan recently lifted its ban on MTBE use in gasoline. In 1995, worldwide demand for MTBE is projected to be between

470,000 and 615,000 barrels/day (241,000–315,000 barrels/day ethanol equivalent). Future capacity is expected to come from the United States, Saudi Arabia, Malaupia, Canada, Venezuela, and Mexico (Stodolsky and Singh 1991).

9.1.2 Tertiary Amyl Methyl Ether (TAME). TAME is not expected to capture a significant portion of the oxygenate market (i.e., approximately 10%) because of the relatively small quantity of C_5 streams (required to produce TAME) that is available in domestic refineries (Wood 1991). However, because TAME is produced from small facilities using in-house feedstocks and not from stand-alone capital-intensive units, it should be cost competitive (API 1988).

9.1.3 Methanol. Methanol, primarily manufactured by thermal processes at rapid rates, can be produced from fossil fuels such as natural gas, petroleum naphthas, and coal, and from biomass resources such as woody and herbaceous plants. Because methanol increases the RVP significantly, methanol is not widely accepted for blending with gasoline in the United States. However, methanol is routinely used on a co-solvent basis in Europe at levels up to 3% in gasoline. In 1988, the worldwide use of methanol as a gasoline additive was 180 megaliters (47 million gallons).

Methanol can be employed directly as a neat (close to 100%) fuel, with many fuel properties that are desirable. Neat alcohols provide superior efficiency and performance to gasoline in properly optimized engines because they require lower stoichiometric air/fuel ratios, have higher latent heats of vaporization, provide higher octane values, and have a lower flame temperature. Thus, methanol is often preferred to gasoline for high performance in automobile races such as the Indianapolis 500.

Currently, mixtures of 85% methanol and 15% gasoline (known as M85) are often preferred over pure methanol for automotive use. The addition of gasoline increases the vapor pressure of the fuel enough to facilitate cold starting. Further engine development is needed to cold start engines with pure methanol, particularly during winter months in colder climates.

9.1.4 Tertiary Butyl Alcohol (TBA). Currently, there is no market for TBA as a gasoline blending agent, and all TBA available for fuel use is converted to isobutylene for MTBE production (API 1988). n-Butanol produced with conventional technology is estimated to cost from $0.69 to $0.82/liter ($2.60/gallon to $3.10/gallon) (1990 $) via synthetic methods (Leeper et al. 1991). Fermentation methods project a cost of butanol of $1.05/liter ($4.00/gallon) (1990 $). Neither of these oxygenates is expected to capture a significant portion of the market because they are not economically attractive compared to other options.

9.1.5 Isopropanol (IPA). Currently, most IPA and TBA is made synthetically; however, both can be produced from biomass using both biochemical and thermochemical techniques. IPA is too expensive to be used as a gasoline blending agent but has been used in gasoline at a concentration of less than 2% to prevent carburetor icing (API 1988). Costs for IPA may decrease, however, as refiners use captive C_4 streams to make MTBE; currently these streams are reacted with propylene (Wood 1991). IPA produced by conventional methods is projected to cost from $0.41 to $0.59/liter ($1.56/gallon to $2.23/gallon) (1990 $) (Leeper et al. 1991). Fermentation derived propanol is estimated to cost from $0.82 to $1.00/liter ($3.10/gallon to $3.78/gallon) (Leeper et al. 1991). Thus, propanols are not cost competitive in the oxygenate market, at this time.

Table 86 presents a comparison of properties for seven oxygenates. As shown, each has potential advantages and disadvantages with no individual option being the best in all categories. Therefore, the transportation and oxygenate markets of the future will likely be met by a mix of fuel choices to meet specific applications.

9.2 Emissions Regulations

Some proponents of ethanol contend that the EPA ruling on reformulated gasoline unfairly discriminates against ethanol because this agreement has no RVP waiver for ethanol blends. Furthermore, they feel the oxygen content of RFG during months with ozone violations may be limited to less than 3.5 wt%. When ethanol is blended with gasoline, the RVP of the mixture increases by about 6.9 kiloPascal (1.0 psi), even though ethanol has a much lower vapor pressure than gasoline. This increase is due to the polar structure of ethanol while gasoline is nonpolar. The incompatibility of the two results in increased evaporation of the components of gasoline such as butanes and benzene. Thus, although ethanol blends reduce tailpipe emissions, evaporative emissions during refueling and running losses are expected to be greater. For ethanol to be blended into RFG, either the unblended gasoline must have an RVP that is about 6.9 kiloPascal (1.0 psi) lower than that required for the final product or else a waiver is required. Because refiners will not likely provide blending feedstock gasoline at a

Table 86. Oxygenate comparison (Piel 1991, Federal Register 1992)

Oxygenate	Economics	Environmental Fuel Properties	Impacts End-Use Emissions	Vehicle Octane Rating	Performance Heating Value	Engine Component Compatibility	Supply	Health & Safety	Government Policies
MTBE	(+) Low - Moderate Cost	(0) Moderate Blend RVP	(0) Inc. NO_x; Dec. CO	(+) 3rd Highest Blend Octane	(0) 3rd Highest LHV	(+) Fungible in wet system	(-) Now all from non-renewables	(-) Effects similar to gasoline	(0) No specific policies
ETBE	DNA (1)	(+) 2nd Lowest Blend RVP	(0) Inc. NO_x; Dec. CO	(+) 2nd Highest Blend Octane	(0) 2nd Highest LHV	(+) Fungible in wet system	(0) Domestic, renewable ethanol feed	(-) Effects similar to gasoline	(0) No specific policies
TAME	DNA (2)	(++) Lowest Blend RVP	(0) Inc. NO_x; Dec. CO	(+) Increased Blend Octane	(+) Highest LHV	(+) Fungible in wet system	(-) Now all from non-renewables	(-) Effects similar to gasoline	(0) No specific policies
Ethanol	(-) Somewhat High Cost	(-) High Blend RVP	(0) Inc. NO_x; Dec. CO	(++) Highest Blend	(-) 2nd Lowest LHV	(-) Not fungible; corrosive	(+) Domestic, renewable feedstock	(+) Biodegradable	(+) Tax incentives
Methanol	(++) Low	(–) Very high Blend RVP	(0) Inc. NO_x; Dec. CO	(+) Increased Blend Octane	(-) Lowest LHV	(-) Not fungible; corrosive	(-) Now all from non-renewables	(-) Toxic: transparent flame	(+) Tax incentives for renewable
TBA	(–) Very High Cost	(0) Moderate Blend RVP	(0) Inc. NO_x; Dec. CO	(0) Lowest Octane Increase	(0) 3rd Highest LHV	(0) Fungible but soluble	(-) Now all from non-renewables	DNA	(0) No specific policies
IPA	(–) Very High Cost	(-) High Blend RVP	(0) Inc. NO_x; Dec. CO	(+) Increased Blend Octane	(0) 2nd Lowest LHV	(0) Fungible, but soluble	(-) Now all from non-renewables	DNA	(0) No specific policies

Notes:
(1) Likely high; depends on ethanol feedstock costs
(2) Likely low to moderate because of in-house use of C_5 streams

NOTE: DNA implies data not available.

lower RVP, the ethanol industry supports an RVP waiver to ensure competitiveness. The EPA, however, does not think that it could legally provide a waiver for ethanol blends because the RFG standard requires a 15% reduction in VOC emissions and provides no RVP waiver.

In the first 2 years of the reformulated gasoline program, the EPA will use an air model known as the Simple Model that uses a mass-based emissions standard to regulate ozone precursors such reactive hydrocarbons. Because ethanol increases the vapor pressure of gasoline, greater quantities of reactive hydrocarbons (on a mass basis) are emitted from RFG with ethanol. Therefore, the 15% reduction in hydrocarbon emissions cannot be met. In later years, EPA may use the Complex Model which uses a reactivity standard to project the impact of emissions of reactive hydrocarbons on air quality. Using this model, ethanol may show improvements in air quality because the lower reactivity of the hydrocarbons released by ethanol blends could more than compensate for the greater quantity that are released. EPA acknowledges that the limited participation of ethanol in early years of the RFG program would likely decrease its use in the future even though the Complex Model may reverse the findings of the Simple Model.

In October 1992, the Bush administration announced that the 6.9 kiloPascal (1.0 psi) waiver will apply to all ethanol-RFG blends for up to 30% of the market in northern cities (Anderson 1992a and 1992b). To compensate for any increase in ozone-forming emissions, the RVP of gasoline will be lowered by 2.0 kiloPascal (0.3 psi) to a RVP of 54 kiloPascal (7.8 psig). Gasoline with this vapor pressure specification is now sold in southern cities in the summer. States may also choose to apply the waiver to more than 30% of the market if they compensate by additional RVP reductions on gasoline. Southern cities can either employ the RFG program as it was originally planned with a 50 kiloPascal (7.2 psig) gasoline or they can apply the waiver to 20% of the market if they reduce the RVP by 1.4 kiloPascal (0.2 psi) to 48 kiloPascal (7.0 psig).

Some of the other features of this announcement include a call for tax legislation to support conversion of ethanol to ETBE. It also ensures that 39 carbon monoxide non-attainment cities will participate in the oxygenated fuels program in the fall of 1992 and discourages states from reducing ethanol use by imposing caps on oxygenate levels.

Another factor working against ethanol is the proposed oxygen limit in RFG of 2.1 wt% during months of ozone exceedances. This oxygen concentration corresponds to an ethanol content of 6% by volume. Ethanol gasoline blends of less than 9.8% ethanol by volume are ineligible for the federal excise tax exemption and thus are less economically attractive. Both of these factors (RVP and oxygen content limitations) may restrict the use of ethanol blends in ozone non-attainment areas. Although

Table 87. Advantages and disadvantages of ethanol from lignocellulosic biomass as a transportation fuel

ADVANTAGES	DISADVANTAGES
Familiar, organic liquid	Raises the RVP when blended with gasoline
Produced from renewable resource	Lower energy content than gasoline; more frequent refueling
Domestic resource base	Initial distribution may be difficult
Few engine modifications required	High flashpoint and wide flammability limits could form flammable mixtures in fuel tank
High-octane fuel	Degrades some elastomers, plastics, and metals
Greater engine efficiency	Cold temperature starts may be difficult as neat fuel
Flexible fuel and dual fuel vehicles available	Corrosive with water
Low toxicity	Separates from gasoline in mixtures when exposed to water
Few driver behavior modifications required	
Lower emissions of reactive hydrocarbons and air toxics	
Emissions are less photochemically reactive for neat fuel	
Potential solution to oxygenate requirements of the Clean Air Act Amendments of 1990	
Reduces carbon monoxide emissions when blended with gasoline	
Contributes little, if any, net CO_2 to atmosphere	
Creates jobs in farm economy	
Re-uses waste products	

the RFG provisions are currently required in only 9 areas nationwide, the other 87 ozone non-attainment areas may choose to adopt these standards or "opt in" regardless of their population. Table 87 summarizes some advantages and disadvantages of using ethanol as a transportation fuel, assuming it can be made at a low cost from lignocellulosic biomass.

10. The Business Venture

The current projected selling price of ethanol from lignocellulosic biomass is competitive with the price of ethanol from corn. In addition, for certain niche opportunities, the projected price of ethanol would be substantially lower and would compensate for the uncertainty in the price estimates and provide a higher rate of return for first-of-a-kind technology.

10.1 Projected Ethanol Selling Price

The technology described earlier represents an enzyme-based process currently thought to be technically viable for production of ethanol from lignocellulosic biomass. It is based on the best available data from bench-scale experiments on each of the process steps as well as information gathered from operating corn ethanol plants. Tradeoffs have been made among operations of each process step to at least partially optimize the economics of the overall process.

Table 88 presents the discounted cash flow analysis for the modified case according to the economic parameters provided in table 82. As summarized earlier in table 85, the projected price of ethanol for this case is about \$0.32/liter (\$1.23/gallon). This is well within the range of the current market price of ethanol from corn of from \$0.30 to \$0.35/liter (\$1.15 to \$1.35/gallon). Thus, at the price projection shown, ethanol could be produced from lignocellulosic biomass at prices competitive with ethanol from corn.

Table 88. Discounted cash flow for ethanol production from lignocellulosic biomass for modified case (all dollars in millions)

Capital Cost	$128.39 MM
Start-up Costs	$6.42
Total Plant Cost	$134.81
Ethanol Selling Price	$0.324/Liter
Production Rate	221 Million Liters/Year

Items	Years																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Percent of Capital Paid	30.0%	50.0%	20.0%															
Capital Invested	$38.52	$64.20	$25.68															
Start-up Cost				$6.42														
Working Capital				$6.31														$(6.31)
Total Annual Capital Outlay	$38.52	$64.20	$25.68	$12.73	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$(6.31)
Total Capital Investment	$38.52	$102.71	$128.39	$141.12	$141.12	$141.12	$141.12	$141.12	$141.12	$141.12	$141.122	$141.12	$141.12	$141.12	$141.12	$141.12	$141.12	$134.81
Percent of Nameplate	0%	0%	0%	60%	80%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Production Rate, MM Liters/Year				132.9	177.1	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4	221.4
Ethanol Revenue				$43.11	$57.48	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85	$71.85
Electricity Revenue				2.49	3.32	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15	4.15
Feedstock Cost				16.13	21.50	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88	26.88
Chemicals. Solids Disposal. Water				5.21	6.94	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68	8.68
Fixed Operating Costs				11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67	11.67
Total Costs				$33.01	$40.12	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23	$47.23
Income Before Depreciation. Taxes				$12.59	$20.68	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77	$28.77
Depreciation				17.18	17.18	17.18	17.18	17.18	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25
Income After Depreciation				$(4.59)	$3.50	$11.59	$11.59	$11.59	$24.52	$24.52	$24.52	$24.52	$24.52	$24.52	$24.52	$24.52	$24.52	$24.52
Income Tax				0.00	1.29	4.29	4.29	4.29	9.07	9.07	9.07	9.07	9.07	9.07	9.07	9.07	9.07	9.07
Income After Tax				$(4.59)	$2.20	$7.30	$7.30	$7.30	$15.45	$15.45	$15.45	$15.45	$15.45	$15.45	$15.45	$15.45	$15.45	$15.45
Total Cash (Depreciation plus Income After Tax)				$12.59	$19.39	$24.48	$24.48	$24.48	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70
Annual Cash Flow	$(38.52)	$(64.20)	$(25.68)	$0.14	$19.39	$24.48	$24.48	$24.48	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$19.70	$26.01
Discounted Cash Flow	$(38.52)	$(58.36)	$(21.22)	$0.10	$13.24	$15.20	$13.82	$12.56	$9.19	$8.35	$7.59	$6.90	$6.28	$5.71	$5.19	$4.72	$4.29	$5.14
Cumulative Discounted Cash Flow	$(38.52)	$(96.88)	$(118.10)	$(118.20)	$(104.96)	$(89.76)	$(75.94)	$(63.37)	$(54.18)	$(45.83)	$(38.24)	$(31.33)	$(25.06)	$(19.35)	$(14.17)	$(9.45)	$(5.17)	$(0.02)

It is important to note that the economic parameters used in this chapter to estimate ethanol selling prices are probably most appropriate for a mature process. However, the technology for ethanol production from lignocellulosic biomass has not yet been fully integrated from front to back of the process at either the bench or pilot scale. Therefore, although the evidence gathered to date is strong that the process flowsheet used to project engineering economics will be verified, uncertainty still exists in the actual process details and interactions. Consequently, the costs could be greater than those used in these projections and/or the performance may not fully meet expectations. In addition, the cost of funds would almost certainly be higher for a first-of-a-kind plant than used in the analyses presented here for an Nth plant to compensate for the additional risk associated with such an investment.

Typically, cost estimates of the type used here have an uncertainty range of about 30% to 40%. Table 89 summarizes the consequences of the cost of capital equipment exceeding the engineering estimates by 40%. Also shown in table 89 is the projected price of ethanol for a 20% real rate of return to the investor. The projected selling price for either scenario exceeds the current market price of corn. As a result, investors may not be willing to invest in a first-of-a-kind process with the projected price so close to the market value of the product.

Table 89. Cost projections for production of ethanol from lignocellulosic biomass for improved technology, additional costs, and niche markets

Process	Plant Size[1] ML/yr EtOH	Capital	Feed	O&M	Electricity	Ethanol
		(1990$/L EtOH)				
Improved	221	0.130	0.121	0.092	0.019	0.324
40% Increase in Capital Costs	221	0.186	0.121	0.095	0.019	0.383
20% Real Rate of Return	221	0.250	0.121	0.092	0.019	0.444
No Cost Feedstock	221	0.128	0.000	0.092	0.019	0.201
Plant Add-on	221	0.072	0.121	0.088	0.019	0.262
Extra Co-product Revenue	221	0.130	0.121	0.092	0.038	0.305
Debt Financing	221	0.081	0.121	0.092	0.019	0.275

[1] Denatured, hydrous ethanol

10.2 Near-Term Market Niches

Several opportunities could be pursued to reduce the cost of ethanol production and provide a buffer for the investor against the uncertainty in the price estimates. The first option is to use a low-cost lignocellulosic waste material that is available in sufficient quantity to support the operation of an ethanol plant. A number of examples of such materials were provided earlier. As shown in table 89, use of a free feedstock would drop the projected price of ethanol by about $0.12/liter ($0.45/gallon) to a cost well below the market price for ethanol from corn.

Another option to lower the cost of ethanol is to reduce the capital investment by building the process as an add-on to an existing plant or by employing used equipment such as from a closed corn ethanol process. To illustrate the impact of this alternative, off site equipment was assumed to be provided by an existing plant, and the discounted cash flow analysis of table 89 was performed with no off site equipment costs. For such a process add-on, the projected selling price drops to about $0.26/liter ($0.98/gallon) even without a low cost feedstock, a price that is once again well below the current selling price range for ethanol from corn.

Increasing the net revenue from co-products will also lower the required selling price of ethanol to achieve a required return on investment. The economics presented are all based on generation of heat and electricity for the process with the solid residue after fermentation and the sale of the extra electricity left after meeting process requirements. It may be possible to obtain higher electricity prices than those assumed in these analyses. It may also be desirable to convert some fraction of the lignin into other products such as adhesives with coal or other fuels used to make up heat and electricity requirements if necessary, depending on the fraction of lignin used. To illustrate such options, the impact of doubling the revenue from electricity sales while maintaining other costs the same is summarized in table 89. In such a situation, the revenue required from ethanol sales can be reduced in direct proportion to the increase in co-product revenue.

An alternative scenario that could provide an attractive approach to reducing the cost of ethanol production is through the use of debt financing for some portion of the ethanol plant. The cost of debt financing is generally lower than for equity funds because debt investors have first priority on the company assets in the event of a business failure. In addition, interest payments on debt are deductible from income before taxes while the net profit of the operation is taxed before return is provided to the equity holders. To illustrate the impact of debt financing on the cost of ethanol production, it was assumed that 80% of the capital equipment costs of the plant were paid from debt with a real rate of return to the debt holders of 5%.

Furthermore, the entire loan was repaid at the end of the plant life. In this case, the cost of ethanol dropped about $0.05/liter ($0.19/gallon) from total equity financing, as shown in table 89.

11. Conclusions

Substantial progress has been made on enzyme based technology for converting lignocellulosic biomass into ethanol. The projected selling price of ethanol has dropped from almost $1.00/liter ($3.70/gallon) 10 years ago to about $0.32/liter ($1.23/gallon) now (all in 1990 dollars), a price competitive with the market range now realized for ethanol from corn. Yet, because the technology has not been proven at a large scale, the price projections are subject to uncertainty, and it may be difficult to finance pioneer plants at prices so close to the market value. However, a number of market niches such as use of low-cost feedstocks, debt financing, higher co-product values, and incorporation into an existing plant could reduce the costs of ethanol substantially and facilitate immediate profitable entry of the technology into commercial markets. The potential to further improve the technology for ethanol production to reduce the price to levels competitive with gasoline without tax incentives promises long-term growth in ethanol markets, particularly to those establishing a technical position early.

In the near term, ethanol will continue to be used as a blending additive with gasoline to boost octane and provide fuel oxygen. Ethanol blends have been shown to reduce emissions of carbon monoxide and unburned hydrocarbons from vehicle exhaust. However, considerable controversy has developed over the impact of ethanol blends on evaporative losses and ozone formation, and the resolution of this issue could have substantial impact on the growth of ethanol markets for blends. Ethanol is beginning to be used to produce the gasoline additive ETBE, which provides similar benefits to direct ethanol blending while meeting gasoline fungibility requirements and reducing smog-forming evaporative emissions as well as those from vehicle exhaust. ETBE could provide a near-term growth market, although ethanol prices will likely have to be lower than for direct blends.

In the longer term, the potential domestic supply of biomass for ethanol production could be more than sufficient to allow displacement of all gasoline used in the United States by neat ethanol. Large-scale substitution of neat ethanol for gasoline would reduce imports of vulnerable supplies of petroleum and decrease the trade deficit. Use of neat ethanol would improve urban air quality by decreasing ozone. Because carbon dioxide is perpetually recycled between biomass, fuel, and carbon dioxide for ethanol production from lignocellulosic biomass, little if any net carbon dioxide is contributed to the atmosphere, thereby decreasing the possibility of global climate change.

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The Production of Biogas from Biomass and Wastes

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Biogas production from biomass and waste is technically feasible due to decades of research and development sponsored by industry and government. Major biogas applications include anaerobic processing of MSW, landfill gas, wastewater treatment and biomass-to-methane systems. For certain applications, biogas production can offer good business opportunities for near-term and mid-term future investments. These areas of potential business opportunity in biogas production are identified and the reasons why certain areas are attractive or unattractive are discussed.

Key words: biogas; anaerobic digestion; landfill gas; municipal solid waste; biomass; substitute natural gas.

1. Introduction

Biogas is a mixture of gases containing mainly methane (50–60%) and carbon dioxide that is produced from a biological process called anaerobic digestion. This process involves the bioconversion of organic wastes and/or biomass crop materials in the absence of oxygen. Because this product can be processed for upgrading to a 97% + methane gas mixture suitable for introduction into natural gas pipelines, biogas is considered to be a potentially important source of "substitute natural gas" or "SNG." Though to most, the technology sounds far removed from the thermal gasification systems normally associated with SNG (such as the conversion of coal via Lurgi gasification), biogas generation schemes utilizing wastes and "energy crops" were pursued in the 1970's and 1980's by government and industry as important components of alternative fuel development. This development effort continues today, even though the principal market incentives or "drivers" have changed.

The main driver for biogas developments in the 1970's was the perceived shortage of fossil fuel supplies brought about by the OPEC oil embargo initiated in 1973. The market climate and tax incentives of the decade to follow encouraged the development of alternative energy sources at prices of two to three times pre-OPEC energy costs. Against this backdrop, biogas generation was viewed as an important potential source of methane and a vital component in an energy strategy aimed at reducing imports of fossil fuels. The technology was also believed to be significant in its potential impact. Several systems studies projected that energy crops produced on less than half the prime agricultural lands set aside in the USDA "Payment In Kind" Program could produce 2.8 to 4.4 EJ of methane per year, or roughly 15–22% of the natural gas consumption of the United States (Lipinsky et al., 1983). The addition of various community wastes (i.e., municipal solid waste, nontoxic industrial solid wastes, commercial wastes, sewage sludge, etc.) significantly increases this methane generation potential. These projections did not go unnoticed and provided much of the rationale for biogas technology development by industry and government in the 1970's.

In the decade of the 1990's, the marketing climate is different and the drivers for further development have changed from an emphasis on "energy security" to drivers related to environmental protection. This means that new business opportunities lie ahead for biogas generation. The purpose of this chapter is to discuss the R&D strategies of the past and present which are aimed at cultivating new markets and the potential business opportunities that lay ahead as a function of energy pricing and other key market factors.

2. Background

Efforts to develop biogas production facilities utilizing biomass and waste feedstocks have generally fallen into three categories. These include: 1) small farm or community-scale systems designed to provide low to medium Btu gas for local heating or electricity, 2) energy farms utilizing dedicated biomass grown in energy plantations for the production of substitute natural gas (SNG) which could be distributed in natural gas pipelines, and, 3) MSW conversion systems which include landfill gas (LFG) and above-ground anaerobic digestion facilities. In the latter category, biogas is coproduced with waste treatment and MSW volume reduction.

In the United States today, despite a major development program in the 1970's and 1980's, little biogas is produced except for use in electricity production. Less than 0.1 EJ of biogas was produced in 1991 compared to over 20 EJ provided by natural gas industry sources. Most biogas used in electric power generation is produced from landfill gas, though commercial technology exists to convert municipal solid waste and industrial organic waste streams to biogas. The numbers of full scale applications of biogas generation in the United States are low even though major technological advances have been made. Market failure resulted from lower-than-expected fossil energy prices, due in part to improvements in drilling and exploration, constrained demand due to conservation, inexpensive imported energy, and economic recession (Lihn and Woods, 1992). This current scenario is in sharp contrast to the outlook in the 1970's when the United States experienced two oil shocks resulting in large price increases for energy and a perceived scarcity of future supplies. Future shocks are not incomprehensible considering the unsettling political climate of the Middle East.

2.1 Current Trends in Perceptions on Renewables

Today, a shift is occurring and there appears to be a reviving interest in using renewables and wastes. This new cycle appears to be fueled by the perception that the domestic United States oil industry is moving overseas as a result of lower production prices in Saudi Arabia and elsewhere and because of increasingly stringent environmental requirements in the United States Current trends predict that imports in the United States will increase from 40% in 1989 to over 66% in 2010 as a result of decreases in domestic oil production (Lihn and Woods, 1992). A study by the American Petroleum Institute (API) predicts that if the Resource Conservation and Recovery Act (RCRA) is strictly applied to the United States oil and gas industry, 8 out of 10 wells producing in 1991 would be shut down, 2.5 billion barrels in oil reserves and 10.8 EJ (1.06 EJ = 1.0 Quadrillion Btu) of recoverable gas reserves would be permanently unrecoverable, and 148,000 jobs would be lost (Brown, 1991). This trend has led to concerns that the chemicals industry, which accounts for the second highest trade surplus in the United States (C/E News, 1992), could be affected by the massive structural changes taking place in the United States petroleum refining industry (Osten and Veno, 1991).

Concerns over the uncertainty of foreign oil supplies have led to a renewed interest in renewables as feedstocks for chemicals and fuels. One logical approach for developing a renewables industry is to establish biomass refineries with multiple products including chemicals, food-related products, and energy. The best example of the biorefinery can be found in the corn wet milling industry which produces high fructose corn syrup and chemicals including ethanol (as an oxygenated fuel additive) in an industry that generates more than $6 billion/year in revenue and utilizes 110 billion Kg (or 12–14%) of the United States corn crop (Datta, 1992). Since biorefineries will need to minimize or eliminate wastestreams, methane may be generated, in some cases, as a byproduct of industrial processes either for energy or as a feedstock for chemical manufacture as one of several product streams.

Another reason for using renewable biomass materials is that there are increasing amounts of land set aside (estimated at 30 million hectares or 78 million acres) through payment in kind programs to farmers (estimated at $10.9 billion/year) which could be used to produce feedstocks for chemicals, fuels or other purposes (Frank and Smith, 1988; Szmant, 1986). Environmentally compatible chemicals and processes are becoming increasingly important, and windows of opportunity are available to produce "green" products from crops and wastes thereby using domestic feedstocks and reducing carbon dioxide production.

These trends will undoubtedly continue over the next decade and will help to shape future markets for various types of biogas generation technologies.

2.2 The Value of Biogas

Economic assessments of the opportunities offered by biogas generation systems must take into account the true value of biogas as a marketable commodity. Since biogas can be introduced into the pipeline as a supplement to natural gas supplies, it follows that biogas must be competitive with the acquisition price of conventional natural gas sources. The cost of producing biogas, therefore, is often compared to the acquisition price of natural gas (i.e., the price that natural gas pipeline companies pay for natural gas supplies) to determine the economic feasibility of various biogas production technologies.

Predictions of trends in natural gas supply and prices are performed on an annual basis by the Gas Research Institute (Holtberg et al., 1992). Trends in United States gas supply for the gas supply sources in the 1992 Edition of the GRI Baseline Projection are summarized in table 90. This table shows United States gas supply growing steadily from 1990 to 2010. By the Year 2000, United States gas supply is only slightly below its previous peak level in 1972, and by 2010, United States gas supply is projected to reach 26 EJ.

Gas acquisition prices in the baseline projection are determined by the competition between gas and other energy supplies (e.g., coal and petroleum). Prices of individual gas sources, however, are driven by competition among these sources. Current gas prices are set mostly by gas-to-gas competition as a result of the abundant supply situation for natural gas, often termed the "gas bubble." This has led to a lower gas price than would be expected to result from the competition between gas and other energy sources. Table 91 shows the trends in gas acquisition prices in the 1992 Edition of the GRI Baseline Projection (Holtberg et al., 1992). Average gas prices are projected to grow steadily during the 1990's, averaging 5.2 percent per year. Acquisition prices for gas increase from an average of nearly $1.70/GJ in 1990 to over $4.20/GJ in 2010.

Processing and transportation add $1–2/GJ to the price of natural gas (depending upon the distances transported and upon the terms of individual contracts). The average price of natural gas at the city gate in 1991 was $3.38/GJ and the average cost to the ultimate customer was $4.39/GJ (AGA, 1991). Ranges for these gas prices on a region-by-region basis throughout the United States are available from AGA price data (AGA, 1991).

Table 90

Gas Supply Trends: 1992 Edition of the GRI Baseline Projection (EJ)

Item	Actual 1990[a]	1995	2000	2010
Lower-48 Production[b]	17.8	17.9	18.8	19.3
Base Technology	(17.8)	(16.8)	(16.2)	(14.0)
Advanced Technology	(-)	(1.0)	(2.5)	(5.3)
Alaskan Production	0.3	0.3	0.3	1.7
Southern[c]	(0.3)	(0.3)	(0.3)	(0.4)
Northern[d]	(-)	(-)	(-)	(1.2)
Pipeline	1.5	2.2	2.5	2.6
LNG Imports	0.1	0.5	0.8	1.3
Coal Gas	0.1	0.1	0.1	0.1
Other Gas[e]	-0.4[f]	0.2	0.2	0.2
Total Purchases	19.2	21.1	22.7	25.1
Lease and Plant Fuel	1.3	1.2	1.3	1.3
Total Supply	20.4	22.4	24.0	26.4
Less: Balancing Item & Exports	(0.1)	(0.5)	(0.5)	(0.5)
Total Demand	20.6	21.8	23.4	25.8

[a] Taken from June 1991 DOE/Eia Natural Gas Monthly published in June 1991.
[b] Lower-48 production does not include lease and plant fuel supplies.
[c] Southern Alaska natural gas supplies were estimated from projected Alaskan consumption.
[d] Northern Alaska natural gas represents supplies delivered to the lower-48 via ANGTS.
[e] Includes 0.5 EJ of net injection into storage.

Table 91

Trends in Gas Acquisition Prices: 1992 Edition of the GRI Baseline Projection (1992$/GJ).

	Actual 1990[a]	1995	2000	2010
Lower-48 Production	$1.63	$2.00	$2.70	$4.08
Northern Alaska	-	-	-	4.52
Pipeline Imports	1.96	2.28	2.97	4.39
LNG	2.18	2.58	3.24	4.59
Coal Gas	2.87	2.87	2.87	3.74
Other Gas[b]	2.86	3.35	4.03	6.30
U.S. Average	$1.67	$2.08	$2.76	$4.19

[a] Price for natural gas supplies consumed in Alaska, lower-48 conventional, and unconventional natural gas supplies using base technology.
[b] Other gas includes SNG from petroleum, propane-air, and refinery gas.

Current and future prices of natural gas at the well head and at the city gate will largely determine the market value of biogas. Biogas that is produced far from the geographic locations of end-use markets (as is the case of biomass plantations) will likely have to compete with well-head prices.

Biogas that is produced from sources within or near cities will likely compete with city gate prices. These comparisons are important considerations in the evaluation of commercial opportunities in biogas generation.

3. Current and Future Markets

A number of biogas technologies developed over the last 20 years as alternative energy sources, still represent potentially important investment opportunities for the near-, mid- and long-term future. However, a good understanding of the different types of technology applications, the nature of the business climate for each application, and the changing market drivers for each application type is needed to evaluate these opportunities. As with any endeavor which promotes new technology, good investments in the area of biogas technologies will depend as much on smart marketing and financial decision-making as on technical success. A good place to begin is to look hard at current biogas process marketing endeavors and determine what are the weaknesses and strengths, the barriers encountered along the way, and the effects of various market drivers on the success or failure of various products. Although this kind of in-depth analysis is beyond the scope of this chapter, the discussion to follow will attempt to provide some initial guide posts that may be helpful in initiating this type of analysis.

The biogas market is not a monolith and no single set of technical, regulatory, environmental and policy drivers controls the commercial destiny of all products. In all, there are more than 50 commercial ventures worldwide that are actively promoting anaerobic digestion technology for biogas generation. The basic types of anaerobic digester design that are commercially available are shown in figure 66. The significant commercial processes currently promoted in the United States and Europe are presented in table 92. As can be seen in table 92, the processes are of widely varied designs varied applications and uses. Over the last twenty years, biogas developments have targeted five categories of applications, including: 1) Manure conversion systems for feedlot and dairy operations, 2) Biomass crop conversion to methane, 3) Anaerobic processing of community wastes including MSW, 4) Landfill gas, and, 5) Wastewater treatment. Each of these categories has its own market drivers, competing technologies, and business climate factors, and understanding each category is essential to recognizing new opportunities for investment in the future. These market categories are discussed in the following sections.

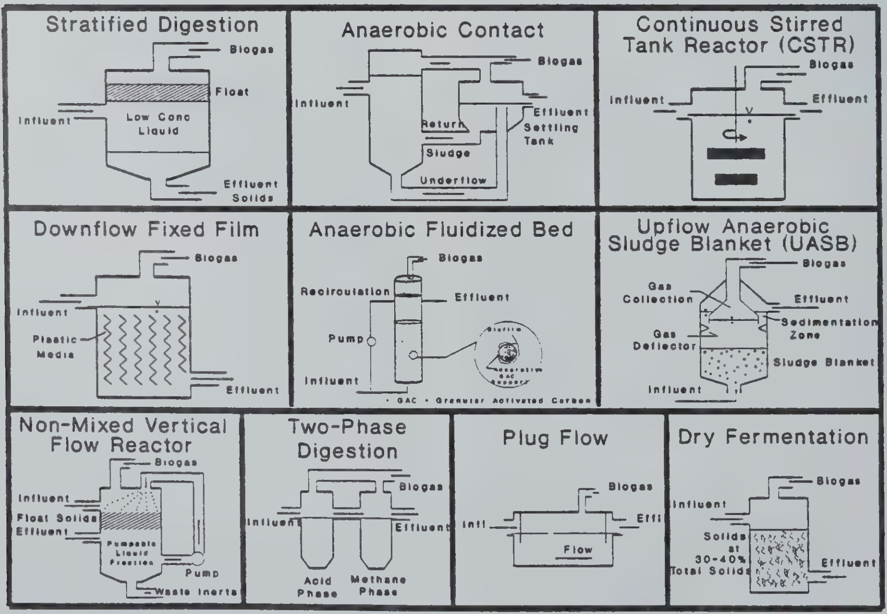

Figure 66. Commercial biogas generation designs.

Table 92

Commercial Biogas Generation Technologies (Continued)

Process	Targeted Market	Promotional Firm	Process Description
BIOTHANE	Industrial Wastewater	Biothane Corporation Camden, NJ	Upflow anaerobic sludge blanket (UASB) process similar to the generic UASB shown in Figure 1.
BIOTIM A	Industrial Wastewater and Municipal Wastewater	Arbios S.A. Charleroi-Belgium	A digester "system" which is comprised of a combination of digester designs such as the upflow anaerobic sludge blanket process, two-phase digestion and Biotim's proprietary process called the CASB reactor which was not described in the vendor's literature.
BVF/HAF	Industrial Sludges, Industrial Wastewater and Municipal Wastewater	ADI, Ltd. Fredericton, New Brunswick	Horizontal plug flow reactor followed by a horizontal fixed film reactor (called the horizontal anaerobic filter or HAF). A generic diagram of the horizontal plug flow reactor is shown in Figure 1.
DRANCO	Municipal Solid Waste	Organic Waste Systems Gent, Belgium	The name "DRANCO" stands for DRy ANaerobic COmposting. The process operates at thermophilic temperatures of 50-55°C with digester contents of 30-40% dry solids and with little or no free water. The process handles a high loading of solids at a short retention time (less than 18 days).
LANFILGAS	LFG	Institute of Gas Technology Chicago, IL	Patented enhancements (including delivery techniques for moisture, nutrients, and buffers) to promote rate and extent of microbial conversion of MSW to methane and carbon dioxide comprise this technology.
ACIMET	Industrial Wastewater and Municipal Wastewater	DuPage Group and the Institute of Gas Technology of Chicago, IL	Two-phase anaerobic digestion. Complex organics are broken down to simple volatile acids in the first stage followed by conversion of the volatile acids to methane and carbon dioxide in the second stage.
ANAMET	Industrial Organic Sludges	AC Biotechnics, Inc. West Woodbury, NY	Anaerobic contact process similar to the generic depiction shown in Figure 1. Schemes can include a combination of mesophilic and thermophilic anaerobic contactors in the system design.
BACARDI	Industrial Wastewater	Bacardi Corporation San Juan, Puerto Rico	Downflow fixed film reactor similar to the generic diagram for the process shown in Figure 1. The reactor is filled with a fixed plastic packing to which films of bacteria are grown. As the wastewater is passed through the reactor from top to bottom, and as wastewater is passed over the biofilms, bacteria convert organics to methane and carbon dioxide.
BIOPAQ	Industrial Wastewater	Paques Lavalin Birmingham, MI Toronto, Ontario	The heart of the patented BIOPAQ system is an upflow anaerobic sludge blanket process (UASB). The UASB is generically depicted in Figure 1. The wastewater to be treated is pumped into the UASB at the bottom of the reactor. As the wastewater percolates up through the granular sludge layer, the anaerobic bacteria convert the organic matter to methane and carbon dioxide.

Table 92 – continued

Commercial Biogas Generation Technologies (Continued)

Process	Targeted Market	Promotional Firm	Process Description
MULTI-ZONE	Landfill Leachates	Zimpro/Passavant Rothschild, WI	A stratified "multi-zone" anaerobic digester. No internal mechanical mixing is used. Fluids in the midsection and top section of the reactor are collected and recirculated through the bottom of the reactor. The reactor seems to have a non-mixed static layer of solids near the top quarter of the reactor and a recirculated section in the bottom half of the vessel.
REX ANAEROBIC FLUIDIZED BED PROCESS	Industrial Wastewater and Municipal Wastewater	Envirex Ltd.	This is essentially a fluidized bed reactor operated in an anaerobic mode similar to the generic depiction of Figure 1. The fluidized bed consists of bacterial films grown on inert particles (e.g. granular activated carbon) which are fluidized by water stream recirculated through the reactor from bottom to top. As the water flows past the biofilms, the anaerobic bacteria convert organic matter to methane and carbon dioxide. Novel process features include biofilm growth control, the selection of the fluidized media, and an improved flow distribution system.
SGN	Industrial Wastewater and Municipal Wastewater	SGN Saint-Quentin-en-Yvelines France	Downflow fixed film reactor similar to the generic depiction of Figure 1. The reactor is filled with a fixed plastic packing to which films of bacteria are grown. As the wastewater is passed through the reactor from top to bottom, and as the wastewater is passed over the biofilms, bacteria convert organics to methane and carbon dioxide.
SOLCON	Municipal Solid Waste and Industrial Sludges and Solid Wastes	Institute of Gas Technology Chicago, IL	Stratified, mechanically unmixed anaerobic digester. Design includes unique fluids management to encourage two-phase digestion in a single vessel. This system includes an optional "Methane Enrichment Digestion" or "MED" feature that has been demonstrated to increase the methane content from 60% up to 95% in biogas generated directly from the digester vessel (Hayes et al., 1990.
VALORGA	Municipal Solid Waste	Valorga Process SA	High solids (28% dry matter) slurry reactor employing no mechanical mixing components inside the vessel but utilizes the sparging of biogas at the bottom of the reactor for mixing, separates liquid from the effluent solids and recycles liquid for combining with the feedstock MSW. This design is similar to the slurry reactor depicted in Figure 1. This reactor can be designed for mesophilic (37-40°C) or thermophilic (55-60°C) operation.

3.1 Manure Conversion Systems

Manure digestion for biogas production has been commercialized throughout the world, in underdeveloped countries as well as developed nations. Nations such as China and India are renown for their simple, batch reactors constructed from crude materials while Europe and the United States have explored numerous digester designs that can be applied at a wide range of sizes. The digester designs that have been promoted most predominantly in the Western World are the plug flow reactor and the continuous stirred tank reactor (CSTR) (Wise, 1981).

Development of anaerobic digestion for farm waste management in the United States dates back to the early part of the twentieth century. One of the earliest efforts in large-impact biogas energy development was aimed at the conversion of animal manures and agricultural crop wastes to methane. Evaluations of crop residues and manure for conversion rates and methane yields were aggressively pursued at the University of Illinois in the 1930's in recognition of the potential of this resource to provide substantial gaseous energy for farms in the United States during the depression (Buswell, 1936). Although some work continued through the decades on anaerobic digestion for application to slaughter house and meat packing waste management, it wasn't until the middle 1970's that the Federal government initiated large scale funding of R&D on anaerobic digestion processing for manure conversion to biogas that could serve as substitute natural gas (SNG). The DOE, in particular, supported a large program in the generation of biogas from beef manure, dairy manure, swine manure, and crop wastes using anaerobic digestion processing. This research also addressed on-farm biogas utilization and a variety of biogas cleanup strategies. Much of this work is described and documented in a CRC Press publication (Wise, 1981). This source contains a wealth of information on laboratory and pilot digestion studies, recommended designs, loading rates, methane yields, conversion efficiencies, residue utilization concepts, etc., related to the digestion of beef manure (Lizdas and Coe, 1981; Coe and Davenport, 1981; Lizdas et al., 1981; Remedios and Boyd, 1981; Prior and Hashimoto, 1981), dairy manure (Jewell et al., 1981; Skrinde et al., 1981; Shelef et al., 1981), poultry manure (Lapp and Robertson, 1981) and crop wastes (Ashare and Buivid, 1981; Young and McCarty, 1981; Pfeffer and Quindrey, 1981).

3.1.1 Resource Base The resource base for agricultural waste residues is large when taking into account all farm wastes, as shown in table 94. It is estimated that crop waste from the production of corn, small grains, sorghum and cotton exceeds 400 million oven-dried Mg per year (Miller and Eisenhauer, 1983; Pimmentel et al., 1981). By comparison, total manure production, including wastes from dairy, beef, swine and poultry operations, totals around 79 million dry Mg per year. The maximum methane production potentials of these resources are shown in table 95. It is estimated in table 95 that if all these residues could be collected and an average of 150 ml of methane could be generated per gram of crop waste and 190–440 ml CH4 could be produced per gram of manure, an annual methane output of over 3,000 PJ per year (3.0 EJ/yr) could be realized having a value of $9–$12 billion per year (assuming a biogas value equivalent to a future wellhead price of $3–$4/GJ). However, because nearly all of the crop waste is highly dispersed, the amount and economics of biogas generation are highly dependent upon a factor called the "collection efficiency" of the resource.

Table 94
Biomass Resource Base for Selected U.S. Farm Wastes

Type of Resource	Annual Generation Rate, 10^6 Dry Ash-Free Mg/Yr	Basis
Crop Waste	410	Small grain, corn, sorghum, cotton and soybean (Miller & Eisenhauer, 1983; Pimentel, et al., 1981)
Manures:		
Dairy Manure	16.7	9.9 million dairy animals[*] 4.3 Kg manure/Mg live wt.
Beef Manure	48.3	100 million beef animals[*] 3.0 Kg manure/Mg live wt.
Swine Manure	6.0	57 million swine animals[*] 3.0 Kg manure/Mg live wt.
Chicken Manure	4.6	1.11 billion birds[*] 6.4 Kg manure/Mg live wt.
Turkey Manure	3.4	107 million birds[*] 6.4 Kg manure/Mg live wt.
Total Manure	79	
Total Waste	489	

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[*] U.S. Bureau of Statistics, 1992.

Table 95
Methane Production Potential for Farm Wastes

Type of Resource	Biomass Generation Rate, millions of dry-ash-free Mg per yr	Methane Yield, liters/Kg	Biogas Generation, PJ/yr	Energy Value, $\$10^9$ per yr[*]
Crop Waste	410	150	2,380	7.1
Manures				
Dairy	16.7	220	135	0.4
Beef	48.3	190	337	1.0
Swine	6.0	370	84	0.2
Chicken	4.6	490'	85	0.2
Turkey	3.4	490	61	0.2
Totals	489	1910	3,082	9.1

---

[*] Assuming an average value of biogas of $3/GJ is realized in biogas sales or utilization.

Achieving crop-waste collection efficiencies of even 25–50% would require substantial changes in agricultural operations where crop wastes are co-harvested with the product and are transported considerable distances (up to 48 Km) to central anaerobic digestion plants sized for handling more than 100 dry Mg/day. A number of studies have estimated that the cost of collecting crop residues and transporting them 15 miles to a central processing facility is significant, costing $11–$21/dry Mg for corn, small grain, and rice residues (Purdue, 1979), $25/dry Mg for sugar cane (Purdue, 1979), and $12–$25/dry Mg for sorghum (Purdue, 1979; Lacewell et al., 1982). These costs are large compared to the biogas revenues for the same crops which are estimated at $13–$17/dry Mg of crop residue (assuming methane yields of 120–190 ml per dry gram and a biogas value of $3–$4/GJ). These comparisons have raised considerable doubt over the economic feasibility of converting crop waste residues to biogas on a commercial scale. This is also evident from engineering analyses that show that even at a 200 MG per day scale, a collection and transportation cost of $22/Mg for corn stover would cause the biogas generation price to increase to above $8/GJ (Ashare and Buivid, 1981).

Manures on the other hand are becoming less dispersed because of advances in agriculture that emphasize controlled, confined feeding operations that employ mechanized manure collection. The collection of manures is generally considered to be more economical than crop wastes, since biomass in the form of animal feed is brought to mechanized feeding operations, including farms and commercial feedlots. Many animal feeding operations employ automated waste removal and manure storage. Therefore, in the economics of manure digestion, the collection of the digester feedstock (manure) is considered to be virtually free. The greater potential for achieving good collection efficiencies with existing infrastructure was one of the compelling reasons why biogas development in the 1970's emphasized manure resource utilization.

If biogas generation is integrated into normal manure collection and handling systems, most applications of agricultural anaerobic digestion facilities will need to be adapted to small- to medium-scale livestock operations (Jewell et al., 1981). Though American agriculture is often considered to be dominated by large agribusinesses, the average size of farms in the United States was 190 ha in 1991. While it is true that there exist large poultry and cattle feeding operations that generate more than 20 dry Mg per day, most farms generate manures at a rate of 0.5–3.0 dry Mg per day. The average dairy farm, for example, manages about 70 cows or less which generate less than 0.5 dry Mg of manure per day. To capture most of the dairy manure resource, therefore, anaerobic digestion facilities need to be constructed and operated economically at a small scale. On the other hand, more than 50% of the manure resource base for beef feedlot operations is associated with large operations managing 4000–32000 head generating 15 to 130 dry Mg per day of manure. Beef operations represented opportunities to realize economies of scale in the implementation of anaerobic digesters which provided a good rationale for beef manure digestion demonstrations in the late 1970's.

3.1.2 Status of the Technology A variety of process designs have been proposed for biogas generation, including the completely mixed (continuous and intermittent) reactor (Marchaim and Criden, 1981), the plug flow reactor (Jewell et al., 1981), unmixed batch digestion (Skrinde, 1981), the semi-continuously fed CSTR (Coe and Davenport, 1981) and combined chemical/biological digestion system (Young and McCarty, 1981). When dealing with manures collected from dirt lots, such as beef feedlots, great care has to be taken in presettling the inert fraction before introduction into the anaerobic digester to avoid excessive accumulations of grit in the digester vessel (Lizdas et al., 1981). Other factors that need to be taken into account in design include ammonia toxicity (especially when dealing with swine and poultry manure) and the careful management of manures from animals that have been given antibiotics.

In the late 1970's and early 1980's, the principal units that were commercially available in the United States for manure conversion to biogas were the intermittently mixed digester which was based on conventional sewage sludge digestion (Langton, 1981; Coppinger et al., 1981) and the plug flow reactor (Jewell, 1981; Fry, 1974). A comparative economic analysis of intermittently mixed and plug flow manure digestion systems based on pilot unit data (28 m^3 reactor volume) has been presented in the literature (Jewell et al., 1981). In a side-by-side pilot demonstration of the two reactors operated on an influent dairy manure concentration of 13% and at organic loadings between 3.5 and 12 kg/m^3-d, the plug flow reactor achieved between 32 and 42% conversion of organics to biogas while the conventional reactor achieved 10–30% less solids conversion. As shown in figure 67, this analysis indicates that for a wide range of dairy farm sizes, from 50 to 300 cows, the plug flow design utilizing an earthen basin and a flexible liner (such as hypalon rubber) is 35% lower in cost than an above-ground intermittently mixed conventional digester constructed from rigid materials. Assumptions for plug flow reactor economics are shown in table 96 and cost breakdowns for the reactor applied to 25–500 head of dairy cows (generating 0.11–2.3 dry Mg manure/day) are given in table 97. Results of this analysis indicated that biogas (50–60% CH4), processed only for water and H2S removal, could be produced at prices from $9.40/GJ for 25 cows down to $2.50/GJ for 500-cow operations (costs adjusted to 1992 dollars). Implementation of the plug flow reactor for very large scale farms of thousands of head of dairy or beef cattle or on swine and/or poultry operations generating more than 5 dry Mg of manure per day, the cost of biogas generation can be accomplished for between $2.00 and $2.40/GJ, depending upon the degree of preprocessing needed for grit removal.

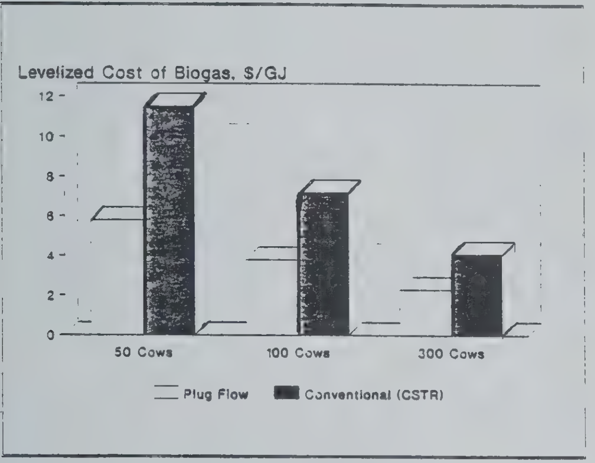

Figure 67. Economics of biogas from manure: Conventional vs plug flow.

Table 96

Assumptions and Inputs Used in the Economic Analysis of the Plug Flow Anaerobic Digester Operated on Manure

Parameter	Value	Comment
Fraction of Net Biogas Utilized	>90%	About 10% of the biogas is used for digester heating.
Annual Interest Rate	8.1%	Based on 15-year historic data.
Annual Inflation Rate	6%	
Life of Loan, Years	20	This is also the equipment life.
Annual Fuel Escalation Rate	6%	
Base Year for costs	1991	

Table 97

Economic Analysis of Biogas Generation on Small Farms ($ 1991).

	Reactor Capacity, Number of Cows Generating Manure Feedstock				
Cost Analysis Parameter	25	50	100	300	500
Net Energy Production, GJ/yr (Determined from energy balance)	203	434	916	2,905	4,924
Capital Cost	$17,800	23,100	31,200	58,300	80,200
Annual Energy Cost (Excluding digester heating)	$40	80	150	450	750
Annual Maintenance Cost	$530	770	1,240	3,110	4,990
Annual Operating Labor Cost	$640	840	1,150	2,180	3,010
Subtotal Annual Operating Cost	$1,210	1,690	2,540	5,740	8,750
Percent Net Biogas Utilized	>90	>90	>90	>90	>90
Cost of Net Energy, $/GJ					
With Operating Labor	$12.10	7.60	5.10	3.40	2.90
Without Operating Labor	$9.40	5.80	3.80	2.30	1.90

All costs in $ 1991.

Since the biogas generation potential from manures is small for most farms (e.g., less than 0.84 m^3 per cow or less than 55 m^3 for a 65-cow dairy farm), most of the biogas will likely be utilized on the farm. Biogas utilization options for the farm include fueling internal combustion engines for electricity generation, water heating and building heating. On the average, only 10% of the total amount of biogas generated is needed for anaerobic digestion process heating; 90% of the gross production is net biogas output. Assuming biogas is utilized on the farm, the cost of biogas generated from plug flow digestion of manure outputs of more than 0.23 Mg (50-dairy-cow equivalent) appears to be competitive with competitive with Number 2 fuel oil (valued at $7.10/GJ at $1.00/gallon) and propane (valued between $6 and $7/GJ). At a scale of less than 0.1 dry ton/day (25 dairy cow equivalent) the cost of biogas (at over $9/GJ) is not competitive. Very large dairy farms of hundreds of head may have excess biogas or electricity produced from biogas that can be sold to utilities; these revenue streams would of course depend upon negotiations with utility companies on the price of the surplus energy products. Biogas generated from digestion facilities processing more than 1.5 Mg/day (equivalent to more than 300 dairy cows) is estimated to cost $3.40/GJ, plus about $2.00/GJ to upgrade the biogas to pipeline quality methane (97% CH_4). The resulting total cost of pipeline quality gas from manure, therefore, is

$5.40/GJ which is uncompetitive with current and projected future acquisition prices for natural gas.

By-product credits for manure utilized for nutrients and re-feedable protein and fiber are valued at no more than $7/dry Mg of manure (equivalent to $1.00/GJ), but more technical and market development are required to realize this revenue stream at full scale. A decision tree of various manure and energy management options for individual farms has been proposed and discussed in the literature (Safley et al., 1976). The technical and economic considerations of converting digester effluent to animal feed has also been discussed (Shuler, 1980).

3.1.3 Market Considerations Potential markets for the application of anaerobic digestion to agricultural operations are considerably large if key barriers to commercialization can be addressed. It is estimated over 75% of farm waste residues are produced on small operations at levels between 0.22 and 3.0 dry Mg per day (Jewell et al., 1981). If 10% of the 2.1 million farms in the United States (United States Bureau of the Census, 1992) implemented manure-based conversion to biogas, a market would exist for the installation of $8–$12 billion of biogas generation and biogas utilization equipment over the next decade. The biogas output represented by this investment is approximately 600–900 PJ/year. There are barriers, however, to realizing this magnitude of market penetration. First, biogas from manure ($5.40/GJ) does not compete with current and future natural gas acquisition prices ($2.00–$4.20/GJ). Biogas generated from manure and upgraded to pipeline quality will cost about $3.00/GJ for the digestion process and $2.00 for gas processing. Second, the generation of farm-based biogas energy, in large part, would be highly diffused—being generated on thousands of farms across the United States having varied access to gas pipelines for direct sale to a gas utility. Low in its availability to the natural gas industry, farm-based biogas would need to demonstrate its benefit in terms of displacing energy forms now used by farms (i.e., electricity, fuel oil, propane, etc.). Companies promoting biogas generation will have to offer biogas utilization systems that allow financial benefits to be realized for more than 90% of the biogas generated on the farm; this means that commercial firms will have to be as effective in the design of biogas utilization concepts as they are in the installation of anaerobic digesters. Initially, this may favor applications for large farms that use heavy amounts of electricity for various year-round purposes such as cooling for product storage (e.g., milk, eggs, etc.) or system mechanization (e.g., waste management, milking operations, etc.).

Another barrier is the up-front capital cost which is about $50,000 for a 1 Mg/day-capacity digestion facility. At a lower scale of 0.22 Mg/day the capital cost is still significant at $18,000. These costs may be difficult to justify for average-sized farm operations with annual net incomes of under $100,000. Companies that offer financing to amortize the capital cost over a period of 5 to 15 years would significantly relieve the first-year cost impediment.

Lastly, there is a need to deal with a confidence barrier that may be encountered throughout the farming community; nonfamiliarity of biological systems undoubtedly breeds skepticism among many in the agricultural community. Perhaps the greatest challenge for would-be commercial promoters of biogas technology in this arena would be to effectively communicate the effectiveness of a few commercial successes and provide educational materials that remove the "mystery" and underscore the practical utility of the technology. Biogas does compete well with the prices paid on the farm for heating oil, propane, and electricity. A strategy that emphasizes on-farm utilization of biogas for energy savings can be one of the most effective (and economically valid) ways of promoting this technology in the agricultural community.

3.2 Dedicated Biomass-to-Methane Systems

A "dedicated biomass-to-methane system" involves the integration of biomass production (aquatic or land-based) with biomass conversion and energy product processing (e.g., biogas upgrading) for the production of methane from "photosynthetically-fixed" solar energy. Over the years, this concept has gained much interest in government and industry as a means of developing a high-impact, renewable sources of methane. Various configurations, ideas and designs have been evaluated by government and industry, but in each effort critical questions have emerged: 1) What can the resource base support as an output of biogas energy? 2) How should a biomass-to-methane (BTM) system be designed to meet regional biogas demands? and, 3) What are the costs? Over the past 20 years, more than $150 million has been spent in R&D by government and industry to answer these questions.

3.2.1 Resource Base Commercial use of biomass for the production of energy now amounts to approximately 2.8 EJ per year or 3.5 percent of the United States energy supply. This market penetration compares favorably with that of nuclear power, which now accounts for 3.1 EJ per year.

Much of the current biomass energy market is involved in the production of electricity from wood and waste (Lipinsky, et al., 1983). This current market is a good indicator of the considerable resource base that can be obtained from the production of biomass.

The potential resource base for biomass production that could be developed for biogas production is generally recognized to be very large. A survey conducted by Battelle Laboratories in the mid-1980's concluded that sufficient land would be available in the United States to produce up to 5.3 EJ of biogas from biomass energy crops without adversely affecting the production of food, feed and fiber (assuming an average biomass yield of only 13–22 Mg ha^{-1} yr^{-1}). In an average year, about 12.2 million ha of prime farmland, approximately 8 percent of the total United States cropland of about 150 million ha, are kept out of production by government programs such as the Payment in Kind (PIK) program that idled 33 million ha in 1983. There is an additional 100 million ha of cropland that is either idle or being used only for pasture (USDA, 1985). Biomass yields of 13–22 Mg ha^{-1} Yr^{-1} on 16–20 million ha of land would produce the biomass resource sufficient for producing 3.4–4.5 EJ per year (Lipinsky et al., 1983).

Several other studies support the significant methane-generating potential of biomass energy. A study conducted by the Office of Technology Assessment concluded that biomass could provide from 4.2–17.9 EJ per year of gross energy for the United States A more recent study by the United States Department of Energy's Research Advisory Board (ERAB, 1982) indicated a net energy potential of 5.3 EJ per year by the year 2000 from biomass systems. These and other studies indicate that land area is not the constraining factor in providing more than 5 percent of the nation's energy demand from biomass resources. As this chapter will show, there are commercial barriers—but land availability is not among them.

3.2.2 Status of the Technology To date, there are no plantation-based BTM systems commercially operating in the United States and Europe. The technology is developmental, mainly proven at the pilot stage for biomass production and conversion.

The development of BTM systems has been an interesting history of government and industrial involvement driven by various perceptions and visions of the future. Though anaerobic digestion has been known to produce combustible gas since the 1850's (Metcalf and Eddy, 1972), the perceived energy shortages of the 1970's first fueled a major institutionalized effort to produce a substitute for natural gas (SNG) from dedicated energy crops. The first modern-day effort was initiated by a visionary, Dr. Howard Wilcox, a distinguished nuclear physicist in the United States Navy, who first advocated producing SNG from seaweeds. The basis for this effort was that fossil energy in the domestic United States was being rapidly depleted, renewable sources of energy needed to be developed but there was not enough arable land available to replace the required demand of domestic energy. Wilcox concluded that the answer lay in the oceans which afforded huge areas which could be fertilized by pumping deep nutrient-rich up-welled water from the depths.

Dr. Ab Flowers from the American Gas Association and later from the Gas Research Institute, was impressed by this concept and initiated support from the United States natural gas industry and later from the Department of Energy. Eventually a multi-million dollar per year program was developed and by the late 1970's General Electric was selected as prime contractor and ocean-grown kelp were being grown in 600 meters of water in a small farm off Newport Beach, California. The concept consisted of growing giant kelp, *Macrocystis pyrifera*, on giant offshore farms, harvesting them periodically with commercial kelp harvesters, and digesting the kelp in inshore anaerobic digesters similar to sewage digesters (conventional stirred tank reactors or CSTR's).

One of the most striking technical difficulties encountered by General Electric and other marine engineers involved with the project was the design of kelp farms in which the kelp did not entangle and eventually damage themselves. The rigid construction of marine structures designed by engineers in the United States, was in marked contrast to the flexible rope farms of the far east (Japan and China) which are used to cultivate hundreds of square miles of seaweed farms as a source of food and chemicals. Despite the lack of success on the production side, progress in anaerobic digestion occurred and several reactor designs were developed which increased solids retention time while decreasing hydraulic retention time. At the same time, it was observed that biomass (i.e., kelp and other land plants) convertability (i.e., efficiency of conversion to methane) was a function of genetics, growth conditions, and harvesting methodology. Convertability turned out to be the most critical cost factor when economic analyses were conducted.

Seaweed cultivation was successfully developed on near-shore farms (Neushul, 1987) or ponds (Bird et al., 1988). This production work eventually lead to successful aquaculture for non-energy purposes (e.g., commercial food production and wastewater treatment). At this time, logistical and engineering difficulties experienced with ocean-based pilot biomass production caused land-based biomass and waste-to-biogas systems to be seriously considered as supplements to fossil fuels.

A general schematic of a land-based BTM system is shown in figure 68. Major components include biomass production, storage (either at the production fields or at the conversion facility), transportation, anaerobic digestion and gas upgrading to pipeline quality (including H_2S and CO_2 separation and moisture removal). Development of this type of system required a comprehensive approach because of the interdependencies of all of the stages of the system. For example, the production of biomass with a certain carbohydrate composition affects its conversion efficiency and methane yield in the anaerobic digestion process. The biomass composition also has an effect on the % methane of the biogas produced by the digestion process (e.g., plants with high fat content will produce higher methane content biogas). Biomass storage design determines carbon losses which affect the net biomass yield. Extensive upgrading of digester gas from 60% to 95% with absorption or membrane systems results in methane losses of up to 10% which require more biomass to meet net methane output targets which increases costs attributed to biomass production, harvesting, and transportation. Other examples abound, but these interdependencies need to be recognized in any BTM development program.

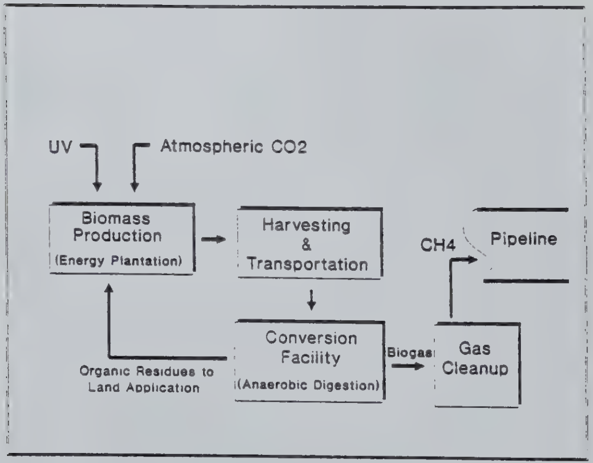
UV
Atmospheric CO2
Biomass Production (Energy Plantation)
Harvesting & Transportation
CH4
Pipeline
Conversion Facility (Anaerobic Digestion)
Biogas
Gas Cleanup
Organic Residues to Land Application

Figure 68. Schematic of a land-based BTM system.

During the 1980's, significant improvements were achieved in land-based BTM technology through the efforts of cooperative research programs between the Gas Research Institute, the State of Florida (University of Florida), the State of Texas (Texas A&M), the State of New York (NYSERDA), and the Department of Energy (the Solar Energy Research Institute). Many of these improvements were achieved through advances in anaerobic digestion technology. Typical organic conversion efficiencies for field crops fed to long-retention-time (>30 days) anaerobic digesters were in the range of 20–50%. Chemical pretreatment approaches (alkaline and acid hydrolysis) were evaluated to improve conversion efficiencies (Young and McCarty, 1981; Pfeffer and Quindrey, 1981), but costs of chemicals (caustics or acids) and heating generally exceeded $3.00/GJ.

In the 1980's, the GRI Biomass Program took a different direction of selecting and developing biomass crops for their high yields and high convertability to maximize energy yields on a net GJ output/ha/yr basis. This finessed approach led to the development of biomass feedstocks that were shown to have more than a 70% conversion efficiency in anaerobic digesters at retention times of less than 15 days; in particular, some varieties of sorghum were converted at an efficiency of more than 80%. Advances with high solids fermentation and with the non-mixed vertical flow reactor (NMVFR) led to increasing allowable loadings from 1.6 to over 8 kg/m^3-d (Jewell et al., 1990; Srivastava et al., 1987). Typical data observed in the pilot scale (4.5 m^3) NMVFR unit at Walt Disney World operated on sorghum are shown in table 98. Further advances in the removal of acid gases from a recycle stream processed in an air stripping or vacuum extraction device, as depicted in figure 69, allows the production of high Btu gas (>90% methane) produced directly from the digester (Hayes, et al., 1990). This process feature, called methane enrichment digestion (MED) has the potential of providing savings of more than $1.00/GJ in gas processing costs in upgrading biogas to a quality suitable for introduction to the natural gas pipeline. Figure 70 demonstrates the advances in digestion technology made during this period.

The GRI program was also able to make considerable improvements in biomass production yields, as well. Energy crops emphasized in this development effort included sorghum cultivars, napiergrass and woody grass. As shown in table 99, production

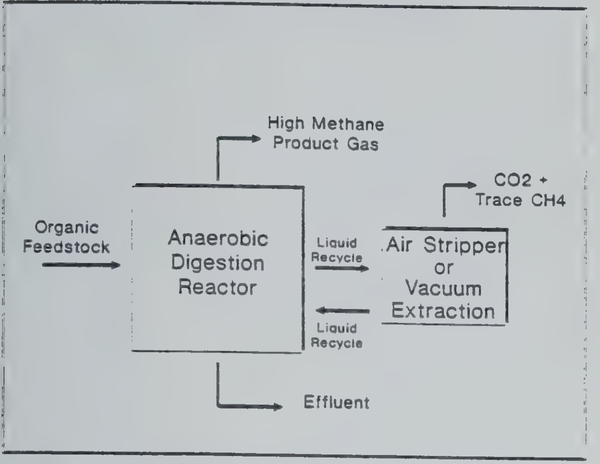

Figure 69. Schematic of methane enrichment digestion.

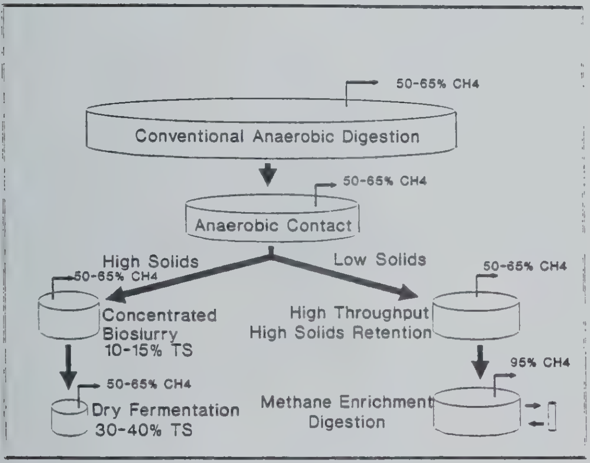
50-65% CH4
Conventional Anaerobic Digestion
50-65% CH4
Anaerobic Contact
High Solids
Low Solids
50-65% CH4
50-65% CH4
Concentrated Bioslurry 10-15% TS
High Throughput High Solids Retention
95% CH4
50-65% CH4
Dry Fermentation 30-40% TS
Methane Enrichment Digestion

Figure 70. Advances in anaerobic digestion.

yields of napier grass and sorghum varieties were doubled over an 8-year period from less than 15 Mg ha^{-1} to more than 35 Mg ha^{-1} (Prine et al., 1988; Smith et al., 1989; Hiler et al., 1986). Low-cost, commercially-available polyethylene bags designed for holding 400 as-received Mg of biomass have the potential of reducing storage costs to less than $7/Mg. This storage technology provides a solution to the problem of seasonal availability of biomass and provides biomass feedstocks to the conversion facility on a year-round basis while keeping biomass storage losses below 5% (Ag-Bag Corp., 1991).

Table 98

Summary of Sorghum Biogasification at the GRI Digester Pilot Reactor at Walt Disney World (Srivastava et al., 1987).

Operating and Performance Parameters	Reactor Experiment 1	Reactor Experiment 2
Scale:		
Total Volume, m^3	4.5	4.5
Effective Volume, m^3	3.9	3.9
Feed Rate, Kg OM[a] day^{-1}	16.8	29.2
Operation:		
Type of Feed	Ensiled Sorghum	Ensiled Sorghum
% TS[b] in Reactor	3.6	6.0
g TS L^{-1}	36	60
Solids Retention Time (SRT), days	18	13
Hydraulic Retention Time (HRT), days	13	10
Type of Process	NMVFR[c]	NMVFR[c]
Performance:		
CH_4 yield, ml/g OM added	331	275
% BMP[d] yield achieved	67	56
Loading Rate, g OM L^{-1} d^{-1}	4.3	7.5
CH_4 Prod Rate, vol/vol/d	1.4	2.0

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[a] Organic Matter = OM.

[b] Total Solids = TS

[c] Non-mixed Vertical Flow Reactor (NMVFR) is commercially available as the SOLCON reactor marketed by the Institute of Gas Technology, Chicago, IL.

[d] Biological Methane Potential: The maximum methane yield achieved in long-term (>60 days) digestion

Table 99

Sorghum Production Yields, 1985 Texas A&M Results (Hiler et al., 1986)

Sorghum		Dry Mg ha^{-1}	% TS
High Energy Test, College Station			
Sweet Sorghum,	Mean	20.8	30.4
	Max (MN1500)	29.3	28.4
Grain x Sweet Hyb	Mean	19.5	35.5
Preliminary Hybrid Trail, Thrall			
Sweet Sorghum,	Mean	17.2	34.4
	Max. (AAtlas x Mn1500)	31.8	38.4
Grain x Sweet Hyb,	Mean	16.8	36.6
Harvest Sequence Study, College Station			
60-45-45 days,	Mean	12.8	14.8
	Max (AT x 623 x Greenleaf)	17.7	17.8
150 days,	Mean	16.8	34.9
	Max (Mn1500)	27.3	35.2
120-60 days,	Mean	25.3	33.1
	Max (Mn1500)	34.9	33.2
60-60-60 days,	Mean	15.5	17.5
	Max (AT x 623 x Greenleaf)	22.0	23.4

These advances achieved through systems-wide R&D approach has allowed substantial progress in reducing BTM costs. In order to allow rapid costing of the BTM system, identify cost sensitivities for prioritizing research, and to quantify the impacts of R&D on BTM system costs, a spreadsheet computer model, called "ECSA" was constructed and used in the management of the GRI Biomass Program. This model was created to provide rapid costing of sorghum, napier grass and woodgrass BTM systems. ECSA is comprehensive and includes conceptual design, mass balances, energy balances, greenhouse gas balances, and costs (±30%) for all components of the BTM system, from the field to the pipeline (Legrand et al., 1988). A cost analysis of an advanced sorghum BTM system is shown in tables 100 through 103 for a 3 PJ/year net output of pipeline-quality gas. Table 100 provides a summary of production and conversion performance information from the GRI R&D program which was used as the basis of the cost analysis. Table 101 lists the economic assumptions used in this analysis. Capital and operating costs for the base and advanced BTM systems are presented in table 102; amortized (levelized) costs are presented in table 103. The costing of this system reflects the economics of one of the most advanced BTM designs should all of the technical improvements be implemented.

Table 100

Input Assumptions for the ECSA[c] Model Describing the BTM Sorghum System

Input Parameter	Value
Production	
Crop Yield, Mg $\mathrm{ha^{-1}\,yr^{-1}}$	30
Total Hectares of Energy Crop	10,600
Percent Crop Coverage, percent	100
Length of Harvest Season, weeks	17
Preconversion Dry Mass Loss, percent dry Matter	7
Fertilizer, Kg Nitrogen $\mathrm{ha^{-1}\,yr^{-1}}$	134
Crop Storage Capacity[a], months	8
Conversion	
Digester Type	NMVFR
Stages	1
First Order Rate Constant (K), $\mathrm{days^{-1}}$	0.075
Temperature, Degrees C	55
Hydraulic Retention Time, Days	20
Biogas Quality, % CH_4	90
SRT:HRT Ratio[b]	2
Feed Mode	Continuous
Feed Conditions	
TPD (dry)	893
Total Solids Content of Sorghum Feedstock, %	22
Total Volatile Solids: Total Solids Ratio	0.95

[a] Assuming the use of polyethylene bags, each storing 400 tons of as-received sorghum.

[b] Solids Retention Time: Hydraulic Retention Time Ratio.

[c] GRI's Energy Crop Systems Analysis Model performs rapid costing of three types of BTM systems.

Table 101

Financial Assumptions Used in the ECSA Cost Model for BTM Systems.

Input Parameter	Value
Base year for cost estimation	1991
Initial year of plant operation	1995
Book life A in years (long term equipment)[a]	30
Book life B in years (short term equipment)[b]	10
Construction period in years	1.5
Constant-dollar discount rate	0.05
Inflation rate	0.06
Current $ escalation rate of by-product value	0.06
Current $ construction cost escalation rate	0.06
Current $ fuel cost escalation rate	0.06
Current $ land cost escalation rate	0.06
Current $ variable O&M cost escalation rate	0.06
Fraction financed by debt	0.65
Fraction financed by common equity	0.00
Fraction financed by preferred equity	0.00
Fraction financed by non-borrowed funds	0.35
Current-dollar return to debt	0.081
Current-dollar return to common equity	0.00
Current dollar return to preferred equity	0.00
Current-dollar return to non-borrowed funds	0.113
Tax life A in years (long term equipment)	15
Tax life B in years (short term equipment)	5
Investment tax credit	0.1
Working capital fraction	0.125
Service factor	0.92

[a] Long term equipment is used in the conversion facility.

[b] Short term equipment is mainly used in agricultural production operations.

Table 102

Capital and Operating Costs for a 3.0 PJ per Year Sorghum BTM System ($ 1991).

Cost Element	Capital ($)	O&M ($/yr)	Labor ($/Yr)	Fuel ($/Yr)
1. Crop Production				
Seed, chemicals		$569,536		
Nitrogen Fertilizer		935,666		
Irrigation water				
Other	$1,495,981	99,732	$1,017,029	$298,328
Total	1,495,981	1,604,934	1,017,029	298,328
2. Harvest and Storage				
Harvesters	4,702,774	767,493	370,365	543,202
Trucks	2,658,879	135,603	740,730	61,530
Silos	761,448	1,287,288		
Total	8,123,100	2,190,383	1,111,095	604,733
3. Transportation				
Trucks	937,764	90,025	256,795	29,474
Front End Loaders	1,178,304	135,741	303,485	89,022
Buffer Storage	21,408	31,958		
Total	2,137,476	257,724	560,279	118,496
4 Conversion				
Digesters	12,376,361	1,831,601		
Ancillary Tanks	2,217,939	414,047		
Heating	414,747	36,075		
Dewatering	4,062,669	247,241		
Mixing		2,048		
Insulation	914,280			
Miscellaneous	17,595,967	71,106		
Total	37,581,962	2,602,117		
5. Residue Recycle				
Lagoon	350,861	8,290		
Irrigation		231,495		
Solid Residue		271,208		
Total	350,861	510,993		
6. Gas Cleanup				
Gas Cleanup	3,633,288	809,029		
Compression	953,100	223,622		
Total	4,586,387	1,032,651		
7. GRAND TOTAL	$54,275,769	$8,198,802	$2,688,403	$1,021,557

Table 103

Present Worth Analysis of a 3.0 PJ per Year Sorghum-to-Biogas System ($ 1991).

Cost Element	Levelized Cost, $/GJ	Percent of Total Cost
Crop Production	$1.19	18.1
Harvest and Storage	2.02	30.9
Transportation	0.48	7.4
Conversion	2.08	31.8
Residue Recycle	0.21	3.3
Gas Cleanup	0.55	8.5
TOTAL	$6.53	100.0

This systems analysis suggests that at the current state of development (advanced case), substitute natural gas could be produced for about $6 to $7/GJ. This price is significantly higher than the anticipated gas acquisition price of $4.40/GJ for the year 2010 (see table 91), but could be competitive with future city gate prices. Further improvements could reduce this cost still further (Legrand et al., 1988). More importantly perhaps, engineering analyses have revealed some hard-won insights into the economics of biomass to methane systems which are counter to some of the intuitive beliefs which fueled research in the 1970's and 1980's. These myths and sometimes counter intuitive findings are shown in table 104.

3.2.3 Market Considerations Today, the economic state of the energy industry makes it highly unlikely that biomass can be used to produce pipeline quality methane as the sole product. Until acquisition prices for methane rise to about $6 per GJ this scenario is unlikely to be taken seriously. It is more likely that methane will be produced as one of the co-products or as a by-product of a modern "biorefinery" in which all product streams are utilized in order to maximize economic payoff and minimize environmental liabilities. As mentioned in the introduction, the corn wet milling industry is the best example of the biorefinery approach and will probably serve as the model for future biomass factories. There is a growing interest in developing new products from biomass in such biorefineries in order to replace petrochemicals with biomass-derived intermediates which can be further processed into biodegradable plastics, "green" solvents, oxychemicals, or direct replacements for petrochemicals.

The production of methane from biomass as a by-product for either direct energy utilization, use as a chemical feedstock (e.g., reforming to CO and H_2), or for use as pipeline-quality methane in a biorefinery scenario could be feasible depending on the product mixture which could be produced (Legrand, 1992). As Legrand (1992) points out, the economics of crude oil refineries are also dependent on the sale of coproducts such as asphalt, lubricants, residual oil, or petrochemicals since only 60% of the crude oil is actually converted to gasoline. In fact, the current interest, public policy support, and subsidies available for liquid fuels such as

Table 104

Fact and Fiction Associated with Biomass to Biogas Research in the 1980's.

Cost Sensitivity	Myth	Finding
Size of Facility	The larger the output of an SNG plant, the greater the economy of scale.	Economies of scale for a dedicated biomass to SNG plant exist up to about four PJ/yr.
Biomass Production Yields (Dry Tons/Acre/Yr)	High biomass yields are needed to greatly reduce methane costs. Earlier beliefs were that over 50 dry tons/acre year were needed.	True until 20-25 dry tons/acre-year. Costs begin leveling off after about 15 dry tons/acre-year.
Farmer Participation in Energy Crop Production	The area around a biomass conversion facility should be planted exclusively in energy crops to reduce transportation costs.	At least one quarter of the area surrounding a biomass conversion facility should be planted in biomass energy crops but there is little economic advantage in planting more than 30% of the area in such crops.
Size of Reactor Vessel	Decreasing hydraulic retention times will result in decreased methane costs (reduced capital costs and size of reactors).	The hydraulic retention time (HRT) can be overdesigned by 50% without incurring more than $0.10/MM Btu (GJ) penalty when HRTs of over 10 days are used. Such a safety factor greatly increases process reliability.
Conversion Efficiency	Increasing the energy content of the crop results in reduced costs of methane.	True. Energy content (convertibility) is the most sensitive cost parameter since it affects both biomass production and methane conversion costs. The design of energy crops for improved convertability is probably the most significant challenge remaining for continued cost reduction.
Thermal Efficiency	Thermophilic operation of digestors results in increased rates of reaction but can lead to energy penalties in colder climates.	Process heat needs for large scale biomass biogasification are very small and could be reduced to nearly zero in any climate.
Transportation of Raw Materials	Significant transportation costs savings can be realized as water content of the biomass is reduced.	True. Significant transportation savings occur between 20 and 35% TS ($1/MM Btu or GJ). Further field drying is not advantageous because of increasing losses.
Biogas Processing	Anaerobic digestion requires an ancillary gas cleanup system to obtain pipeline quality gas since biogas generally contains 50 to 60% methane.	Anaerobic digesters can obtain greater than 95% methane without an ancillary gas cleanup system by proper digester design. Hayes et al (1988) have developed and patented a pH/pressure swing reactor which can produce 95% methane at a cost savings of $1/GJ over conventional systems. This system has been tested successfully at the pilot-scale with municipal solid waste as the feedstock.
Process Type	Anaerobic digester type will greatly affect the economics. CSTR's are the least efficient because they don't retain solids.	True. Most reactor designs were improvements over the CSTR ($1/MMBtu) but no significant economic difference was observed among the various non-CSTR reactors which retain solids.
Technology Advances	Improvements are mainly achievable through fundamental research to reduce costs below $6/MM Btu.	Engineering advances (biomass transportation, reactor optimization, effluent dewatering, etc.) can have as large an impact on costs as more fundamental research.

ethanol, has spurred the production of ethanol as a fuel additive in the United States. It is likely that a similar program of subsidies would be needed to develop pipeline quality methane on an appreciable scale. This would be unlikely since natural gas (or methane) is primarily produced domestically while liquid fuels are increasingly imported from abroad. On the other hand, if a carbon tax were instituted on the basis of carbon dioxide production potential, increased demand for methane, if large enough, could make substitute natural gas (SNG) from biomass sources a more attractive proposition. According to Legrand (1992), if all petroleum were replaced by biomass (which would require about 49% of the 1987 United States cropland or about 80 million hectares), carbon dioxide production would decline from 2.5×10^{15} grams to about 0.3×10^{15} grams. If the 30 million hectares of land currently being subsidized for not growing crops were utilized, carbon dioxide production would decline by about 40%. If prices for energy increase as a result of public policy decisions, if natural gas demand increases because of its lower carbon dioxide emissions, and if subsidies for not growing crops are shifted to crop production for new nonfood products then it is more likely that methane will become a more attractive product from biomass materials. This could also take place, as it did in the late 1970's, if there are disruptions of imported oil due to geopolitical forces and government policies or if demand for methane outstrips either new production or delivery systems. Large-scale energy plantations could be commercially viable if long-term gas acquisition prices rise to levels of $5 to $6 per GJ or higher.

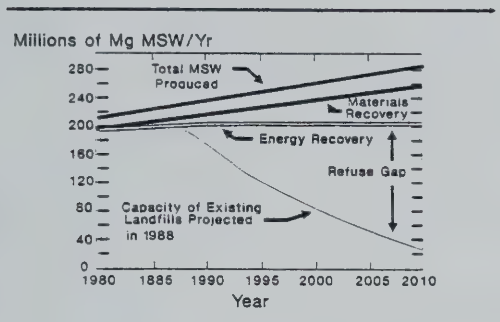
In the near-term, it is likely that biogas production will be attractive when it is a by-product of other processes such as waste treatment (e.g., anaerobic digestion). In the mid-term, methane produced as a co-product by biorefineries will provide the most attractive opportunity for biomass to methane systems. For the longer-term, public policy decisions like those which have been made with respect to ethanol will be needed that reduce dependence on fossil-based fuels and encourage the production of energy from domestically grown biomass and waste materials.

Despite the fact that the production of biogas is currently uneconomical for SNG production at today's energy prices, optimistic future projections suggest that even with new technology reducing the costs of production and improved drilling success rates, there will still be a need for 1 to 2 EJ of supplemental gas (Lihn and Woods, 1992). Conventional wisdom is that this gas will be supplied by unconventional sources of natural gas rather than biomass or coal gasification (Lihn and Woods, 1992). If, however, SNG from biomass is to be widely used as a significant energy source, natural gas acquisition prices would probably have to rise to $6 to $7/GJ (Frank and Smith, 1986), though some estimates suggest that pipeline quality biogas could be produced for around $3 to $4/GJ Btu with further technology improvements. Many of these improvements have already been demonstrated in the laboratory or at the pilot-scale (Legrand et al., 1988).

In summary, the production of biogas, except as a by-product of another process (e.g., waste treatment) is not currently economical. Some technology, however, which was first developed for biogas production (e.g., bioreactors with solids retention) has now been developed commercially for purposes other than energy production (e.g., waste treatment). Though current natural gas prices are below those which could support any kind of substitute natural gas facility (SNG), there are commercial opportunities to utilize gas produced as a by-product of waste treatment systems. Furthermore, as a result of major technical advances in the 1980's, the price at which biogas may be produced from biomass is in the range of $6 to $7/GJ or less rather than the $12/GJ or more which would have been required a decade ago (Smith and Frank, 1988).

3.3 Anaerobic Bioconversion of Community Wastes

The generation of solid wastes has grown considerably over the past three decades to over 2–3 Kg per capita per day in most regions of the United States (Corbitt, 1989) placing this problem among death and taxes as another of life's unavoidable challenges. The United States output of solid waste now totals over 220 million Mg per year and is increasing by about 1 percent per year. Landfill capacity required in the coming years is equal to the total produced minus the materials recovered minus the MSW dedicated to energy recovery; projections for these parameters are given in figure 71. Compounding the problem of growing MSW output is the lack of land area in many populated regions of the United States and the "NIMBY" ("Not In My Back Yard") stance that many communities have taken has curtailed the construction of new landfills required to satisfy disposal needs. This situation has underscored the need for waste reduction and disposal technologies that are



Reference: Earle, 1989

Figure 71. Increasing U.S. output of MSW and decreasing landfill capacity.

environmentally sound, mitigate landfill space requirements, and that are well-received by the community.

3.3.1 Resource Base The amount of community wastes that can be made available for biogas generation is potentially substantial. Assuming that 75% of the total MSW output is accessible and that on the average about 70% of the MSW is composed of convertible organics with a water content of 35%, the amount of MSW feedstock available each year is calculated as follows:

$$\text{Total dry ash-free Mg of MSW/yr} =$$

$$\text{Total MSW Mg/yr} \times 0.75 \times 0.7 \times 0.65 =$$

$$220 \times 10^6 \times 0.5 \times 0.7 \times 0.65 =$$

$$75 \times 10^6 \text{ dry ash-free Mg}$$

Since overall conversion efficiencies of MSW in anaerobic digestion can typically reach more than 65%, the net methane yield amounts to about 280 ml/dry ash-free gram of feedstock (4.5 ft^3/pound). The heating value of 26.7 m^3 of methane is 1 GJ. The amount of biogas that can be potentially generated is calculated as follows:

$$\text{Total } CH_4\text{, PJ/Yr} = 75 \times 10^6 \text{ Mg/yr} \times 10^6 \text{ g/Mg} \times$$

$$280 \text{ ml/g} \times 10^{-6} \text{ m}^3\text{/ml} \times (26.7)^{-1} \text{ PJ/m}^3$$

$$\text{Total } CH_4 \text{ from MSW, PJ/Yr} = 780 \text{ PJ/yr}$$

This methane generation potential is significant since it is equivalent to about four percent of the total natural gas sold in the United States each year. Therefore, if biogas is upgraded to pipeline quality methane and sold as a substitute natural gas commodity at a city gate price of about $3/GJ (the average United States city gate price of gas is $3.40/GJ), the revenue generated from 780 PJ/year would amount to about $2.3 billion per year.

3.3.2 Status of the Technology The state of development of anaerobic digestion technology for handling MSW, sludges and non-hazardous industrial solid wastes is at a relatively high level with many improvements in the technology that have extended the capability of the process to handle a wider range of feedstock types and concentrations. Textbook applications of anaerobic digestion processing in the 1960's, for example, mainly dealt with industrial and municipal sludges of fairly homogeneous consistency with concentrations of 1–4 percent. Today, because of breakthroughs made through research, anaerobic processes can operate on feed streams with organic concentrations of as low as .01% to more than 40%. Digesters today can now handle a variety of streams from dilute wastewater to dry organic solid materials upon which one could walk. Technical improvements are continuing in areas of process stability and rates of biotransformations. New digester designs at the pilot scale have even led to digesters that produce 95% methane directly from the digester itself (Hayes et al., 1990).

Solid waste to biogas systems involve four parts: 1) preprocessing including separation of the biodegradable organic fraction (paper, garbage, cardboard, etc.) from glass and metals, 2) anaerobic digestion, 3) residue management including dewatering, recycling of water and nutrients to the feed end of the anaerobic digester, and effluent solids disposal, and 4) biogas processing and utilization. A schematic of a generic MSW biogas plant is shown in figure 72. Excellent descriptions of the MSW biogas system and the anaerobic digestion processes that can be incorporated into it are provided in a University of Florida technology transfer document which is available to the public upon request (Earle, 1989).

Preprocessing is needed to prepare the MSW before feeding it into the anaerobic digestion process. The composition of MSW is summarized in table 105. Municipal solid waste consists of a number of fractions that need to be separated into component parts before any conversion technology can be applied. These fractions include biodegradable organics (paper, garbage, protein, etc.), nonbiodegradable organics (plastics), inerts or

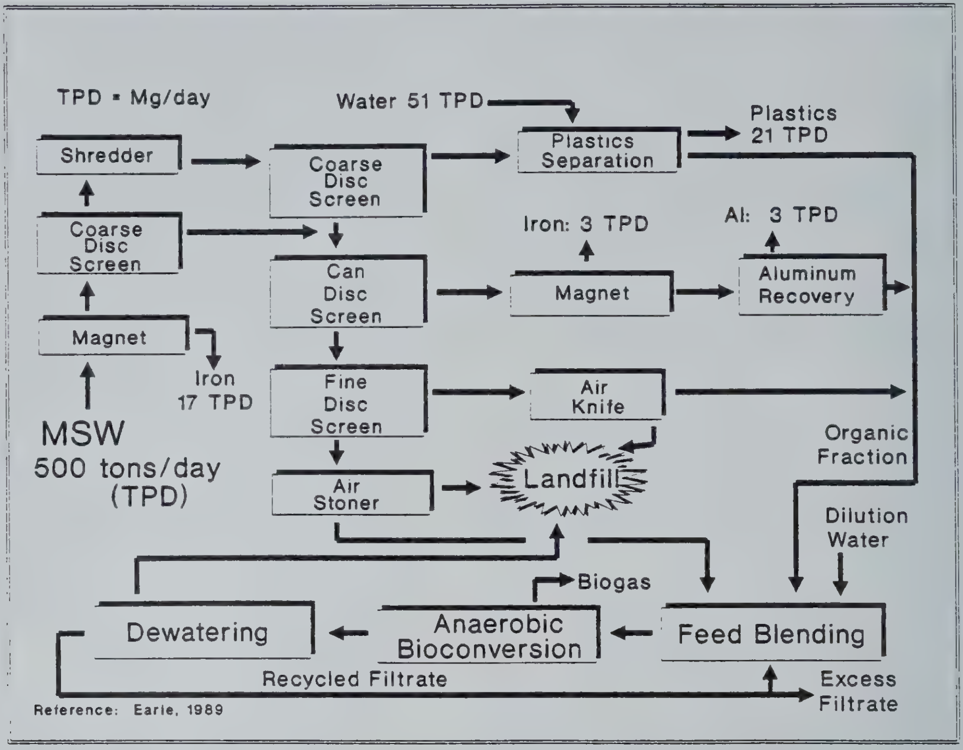


Figure 72. MSW to biogas system.

inorganics (the ash fraction, glass, metals, etc.), and moisture. The objectives of preprocessing include: 1) removal of mechanically troublesome objects (large objects, long stringers, and other things which can interfere with conveying, mixing, pumping, etc.), 2) size reduction of the remaining stream to facilitate materials handling and increase particle surface area to enhance conversion, 3) recovery of recyclable materials such as ferrous metals, aluminum and glass, and 4) removal of biologically inert material (rocks, bricks, concrete, etc.) which is of no use to the bioprocess. The costs of these operations are described in the literature (Legrand et al., 1991).

Technologies to perform separation functions ancillary to anaerobic digestion are available and well known by companies in the United States and Europe experienced in MSW size reduction and sorting. Size reduction is performed with a shredder which can be of the flail, shear or hammermill type. Sorting is often accomplished with screens complemented with magnetic metal separators and some aerodynamic devices for supplemental separation. However, most effective sorting for anaerobic digestion feedstock is performed on the basis of particle size and not density. Disc screens have been found to be particularly appropriate for preparing digester feeds. Likewise, posttreatment residue management processes involving dewatering (e.g., screwpresses, beltpresses, landfilling, combustion, etc.) and disposal are commercially available and well understood in application.

Table 105

Typical Analysis of Municipal Solid Waste (MSW)

Type of Analysis/Constituent	Composition of Raw MSW % by weight	Composition of Refuse Derived Waste (RDF) % by weight
Material		
Paper	43.0	74.0
Plastics	3.0	3.4
Rubber, Leather	2.0	1.9
Wood	3.0	2.8
Textiles	3.0	4.3
Yard Waste	10.0	9.4
Food	10.0	3.4
Fines	10.0	0.6
Glass, Ceramics	9.0	0.04
Metals: Ferrous	6.0	0.21
Aluminum	0.7	0.01
Other Nonferrous	0.3	0.07
Ultimate Analysis		
Carbon	25.6	33.8
Hydrogen	3.4	4.4
Oxygen	20.3	27.9
Nitrogen	0.5	0.5
Chlorine	0.5	0.5
Sulfur	0.2	0.2
Inorganics	24.4	7.3
Moisture	25.2	25.2
Higher Heating Value, Btu/lb	4450	5840

Source: Earle, 1989.

Posttreatment of biogas to upgrade the methane content from 50% to more than 95% (pipeline quality) to make it suitable for sale to a natural gas utility can be performed with a number of commercial processes. The carbon dioxide content of biogas, accounting for 40–50% of the gas volume, can be removed with: 1) solid bed adsorption operated in a temperature swing or pressure swing mode (available from GEMINI), 2) semipermeable membranes such as the spiral wound (Membrane Research and Technology), hollow fiber (Monsanto/Permea) or the tubular types, and 3) absorption/desorption based on pressure swing (e.g., Selexol). The technical and economical aspects of these biogas separations systems are discussed in the literature (Ashare, 1981).

Biogas generation from MSW processing in above-ground reactors has become a well-developed technology which competes well with alternative conversion systems. If generation of energy from MSW is the prime objective, technologies that compete with anaerobic digestion include "refuse derived fuel" (RDF) burning and landfill gas recovery. Landfill gas (LFG) recovery will be described in the next section. The main advantage of landfill gas is that capital for above-ground equipment and processing is greatly reduced. Principal disadvantages are that methane collection systems are often inefficient, the product gas often contains significant amounts of nitrogen gas which increases gas cleanup costs, and conversion rates are slower than above-ground systems. RDF burning is used throughout the United States and is a mature technology that significantly reduces the volume of waste to be landfilled. Although combustion facilities have faced increased opposition from environmentalists and the general public (especially NIMBYs), RDF technologies can potentially meet all Federal and state emission regulations and guidelines for air, water, and ash disposal (Earle, 1989). In some cases, RDF facilities have provided significant savings to the public. Public perception, however, has been a serious constraint to the construction of new RDF facilities in recent years.

Anaerobic digestion processes have been commercially available for solid waste reduction since the mid-1980's; however, most of this initial commercial activity was confined to Europe. Though for more than 50 years, anaerobic digestion has been used extensively in the United States for sewage sludge reduction, commercial digesters have only recently been promoted in this country for the processing of MSW. Europe, on the other hand, has been a leader in the commercialization of various solid waste digester designs including dry anaerobic composting, high concentration slurry reactors and two-phase digestion as seen in figure 1. Europe's lead over the United States in this commercial arena has occurred for a number of reasons including: 1) a higher dependency on foreign oil which has elevated the strategic importance of alternative fuels in Europe, 2) higher fossil fuel prices which have made alternative energy sources more competitive in Europe, and, 3) severe land space constraints for new landfills coupled with negative reactions in many areas in Europe to MSW incineration (i.e., continental NIMBYs).

3.3.3 Market Considerations The conversion of MSW to biogas in above-ground anaerobic digestion facilities is one of the most economically-attractive, near-term, renewable energy options for two important reasons. First, higher credits for biogas generated from MSW will be substantially higher because the MSW conversion facility will almost always be located in or near cities. The biogas from these facilities will have to compete with city gate prices (averaging about $3.40/GJ) rather than well head prices (which now average around $2.10/GJ as shown in table 91). In contrast, biogas from manure or biomass plantations will be produced in agricultural regions of the United States far away from the cities, will require considerable transportation, and will likely compete with well-head prices (now averaging $2.10/GJ). Second, very high credits amounting to over $25/Mg can be obtained for tipping fee charges for processing the MSW. Such waste disposal charges cannot be taken for dedicated biomass plantations and are difficult to take in the processing of most manures and field wastes.

The amount and value of energy products that can be produced from MSW-to-biogas plants will depend on the commercial system design, the energy forms produced and the price that can be obtained from each energy form. Biogas plants have the options of producing at least three energy forms: 1) substitute natural gas, 2) electricity produced from a biogas-fueled gas turbine, and, 3) steam. Comparative economic analysis of MSW conversion to each of these energy forms has shown that in many cases, in today's economy, the best opportunities lie in providing electricity if the commodity can be sold for at least 6 cents/KWH (Legrand et al., 1991; Earle, 1989) and in direct sales of biogas and SNG if a price of at least $3/MSCF can be obtained. These break-even energy revenue requirements are relatively low because of a tipping fee credit exceeding $25/Mg which is equivalent to more than $2.40/GJ.

The economics of biogas generation from MSW has been described in some detail by Legrand et al. (Legrand et al., 1991). A general flow scheme of a 500 ton per day MSW-to-biogas plant is shown in figure 72 and is based on the design and operational assumptions of table 106. The scheme assumes the use of a high-solids CSTR digester operated at feed concentrations of over 16% and loaded with the organic fraction of the MSW at a rate of 6.4 Kg/m^3/day.

Table 106

Base Case Assumptions Used for Mass and Energy Balances and for Economic Analysis

Parameters	Value
Dry Matter Contents	
MSW	74.0% TS
RDF	62.3% TS
Digester Influent	16.2% TS
Digester Slurry and Effluent	8.1% TS
Filtrate Liquid	2.0% TS
Dewatered Filtercake	50.0% TS
Anaerobic Digestion Parameters	
Reactor Type	CSTR
Temperature	60°C
Volatile Solids (VS) Loading Rate	6.25 g VS/liter/day
Hydraulic Retention Time	21 Days
First Order Reaction Rate Coef	0.155 Day^{1}
Methane Yield	0.31 liter CH$_4$/g VS added
Methane Production Rate	1.9 vol/vol/day
Biogas Methane Content	55%
Economic Assumptions	
SNG Sales Price	$2.84/GJ ($3/mmBtu)
Electricity: Purchase	$0.06/KWH
Sale	$0.03/KWH
Final Residue Hauling and Landfill	$33/Mg ($30/U.S. ton)
Aluminum Sales Price	$551/Mg ($500/U.S. ton)
Compost Preparation, net cost	$11/Mg ($10/U.S. ton)
All Cost Escalators	5%/year
% Municipal Ownership	100%
Bond Financing Cost	40% of Capital Cost

Typical costs and revenues are summarized in table 107 where two cases are examined (Legrand, et al., 1991). In one case, it is assumed that biogas is generated from MSW via anaerobic digestion, biogas is sold to the local utility, and the dewatered residue is burned and power is generated. In the second case, it is assumed that the residue is refined into a compost. These are constant-dollar costs of service including the debt amortization and all operating costs, assuming full municipal ownership. As shown in table 107, tipping fees of more than $38/Mg are required along with SNG sales of nearly $15/Mg and by-product credits of $4/Mg (recycleables and electricity) to break even with the costs, the largest of which is the residue incineration system. The second case requires far less tipping fee, less than $26/Mg, because composting equipment is less than half the cost of residue incineration.

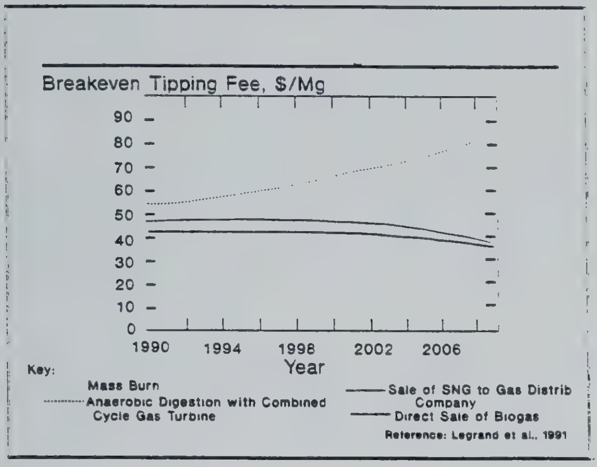
Table 107

Levelized Costs for MSW Biogas Systems (Legrand, et al., 1991).

Item	Constant $/Mg MSW (1988 $)	% of Total Cost
Case I: Residue Burned		
Costs		
MSW preprocessing	14.5	25.4
Anaerobic digestion	10.7	18.7
Gas cleanup	2.8	4.9
Residue burning	18.0	31.5
Landfill costs	11.1	19.4
Total Cost	57.1	100
Revenues		
SNG Sales	14.7	25.7
Electricity and recycleables	4.1	7.2
Tipping fee	38.3	67.1
Total Revenue	57.1	100
Case II: Residue Composted		
Costs		
MSW preprocessing	14.5	32.5
Anaerobic digestion	16.0	35.9
Gas cleanup	6.6	14.6
Residue processing	7.6	17.0
Total Cost	44.7	100
Revenues		
SNG sales	14.7	32.9
Electricity and recycleables	4.1	9.2
Tipping fee	25.9	57.9
Total Revenues	44.7	100

In another analysis, Legrand (1991) presents various sensitivity relationships between cost and key parameters such as digester solids retention time and conversion rate. The analysis also presents life-cycle costs for four types of energy systems including: 1) mass burn for electricity production, 2) anaerobic digestion with electricity production from a biogas-fired combined cycle gas turbine, 3) direct sale of the biogas as a medium Btu fuel, and, 4) cleanup of biogas to pipeline quality and sale of SNG to a gas distribution company (Legrand et al., 1991).

A comparison of the life-cycle breakeven tipping fees for each of these options is presented in figure 73. These curves indicate that the best economies of operation may exist for biogas plants that involve direct sale of biogas either as a medium Btu fuel or as SNG (biogas upgraded to 97% methane) provided the gas can be sold for $3.00/GJ. This price appears to be competitive with the average United States city gate price of $3.40/GJ. But local natural gas prices vary widely from region to region, and considerable analysis needs to be conducted on a regional basis to determine the extent of the potential market for supplemental supplies of SNG from MSW. If over the next 10–20 years the city gate



Reference: Legrand et al., 1991

Figure 73. Life-cycle analysis of mass burning and anaerobic digestion.

price of natural gas exceeds $4–$5/GJ, direct sales to the gas utility in most areas of the United States could provide a significant economic driver for implementing the technology for SNG production. Should no local market in a particular region exist for direct biogas sales, electricity generation using the biogas-fired combined cycle gas turbine appears to have lifecycle cost advantages over mass burn by an average of 11% (breakeven tipping fee basis). Electricity production appears attractive particularly in regions with high electricity costs where power produced by biogas can be sold for 6 cents or more per KWH (Legrand, et al., 1991).

Today, however, the United States remains in an era of cheap fossil fuel energy prices that are at or below the levels of the Arab Oil Embargo of 1973; energy production, therefore, is still not the major market driver for MSW-to-biogas technologies. Other market drivers have, in fact, emerged that can be argued to be more important than energy. These include: 1) reduction of MSW volumes to conserve landfill space, 2) removal of water-soluble constituents that pose a groundwater contamination potential in landfills, and 3) control of methane as a greenhouse gas pollutant.

Depending upon the inerts content of the solid waste and the amount of material recovered through waste reduction or recycling, landfill life can be extended by a factor of 3 to 5 through the implementation of MSW-to-biogas systems (Earle, 1989; Legrand, 1991). Plastics management has a large impact on landfill life; landfill life is greatly extended if plastics are recycled or combusted.

Equally important is the control of many types of water-soluble pollutants that are leached out of the MSW upon landfilling. Rainfall flowing through the soil and landfill materials can leach organic acids, phenols, terpenes, and other organic pollutants from MSW and contaminate surrounding groundwater (Reinhard, 1984). Anaerobic digestion is capable of destroying more than 90 percent of these readily soluble organic compounds that represent a serious source of groundwater pollution. Predigestion, therefore, can largely prevent the deleterious effects of landfills on groundwater supplies.

Likewise, anaerobic digestion can also significantly reduce the potential of MSW to produce greenhouse gases upon landfilling. The "greenhouse" effect or "global warming" phenomenon has recently received a great deal of attention in scientific and public policy circles. These terms refer to a cause-and-effect relationship in which "heat blanketing" of the earth, due to trace gas increases in the atmosphere, is anticipated to result in global warming. Gases suspected to contribute to this effect include carbon dioxide and methane; these gases have increased in concentration, due in part to human activities. Gas from landfills has been recognized to be one of the significant sources of methane to the atmospheric buildup (Bingemer and Crutzen, 1987).

These multiple market drivers coupled with a vast MSW management point to MSW-to-biogas technology as one of the best near-term biotechnology investment opportunities for the future. The growth of MSW production represents both a daunting disposal challenge and a significant source for substitute natural gas through conversion to biogas. A sharp eye on the progress of commercial efforts in Europe can provide a guide to the do's and dont's for technology implementation and market introduction in the United States.

3.4 Landfill Gas

Another biogas technology that has gained much commercial interest is the enhanced production and recovery of biogas from landfills. The same bacterial process of anaerobic digestion that occurs in above-ground commercial reactors can occur in the subsurface of landfills. Once organic materials are deposited into a landfill and covered with properly compacted soil, aerobic soil microorganisms quickly use all available oxygen in landfill materials and anaerobic bacteria, which require oxygen-free conditions to thrive, begin to slowly degrade the organic fraction of the landfilled MSW. The anaerobic bacteria, as previously described, convert organic matter of MSW to biogas, a 50/50 mixture of carbon dioxide and methane. Under normal landfill conditions, in-situ anaerobic digestion occurs very slowly; enhancement techniques employing methods such as water management and nutrient addition can greatly enhance the process. Biogas produced in landfills is called landfill gas or LFG.

3.4.1 Resource Base Landfills generally produce a biogas output amounting to less than 0.05 volumes per volume of MSW per day compared to above-ground anaerobic processes that achieve more than one volume of biogas per volume of reactor per day. But a low biogas generation rate per unit volume of solid waste multiplied over millions of cubic meters of landfill space can amount to a significant output of biogas. It is estimated that a total of five billion Mg of MSW was deposited in landfills throughout the United States since 1960 (Berenyi and Gould, 1992). Researchers have estimated that sanitary landfills in the United States produce approximately 200 PJ of methane per year (Berenyi and Gould, 1992) which indicates the potential size of the landfill gas resource and the magnitude for greenhouse gas emissions if not collected.

3.4.2 Status of the Technology Normally, landfills do not attempt to capture LFG as an energy resource. Because of the highly dispersed nature of its generation and because of energy recovery economics, LFG at many landfill facilities has been collected and flared as a safety precaution to avoid the buildup of methane gas in soils and in the basements of nearby houses. This management practice is now mandated by many state and Federal environmental agencies.

In a typical LFG facility, a closed landfill is capped with an impermeable surface of dirt or clay. Wells of 30–100 feet deep are drilled into the landfill and a vacuum is established in the wells to direct the LFG into the wells. Care is taken to avoid the introduction of air into the landfill that can be caused by pulling a high vacuum on the gas interdiction wells. Gas removed from the landfill contains 50–60 percent methane and has a heating content of around 19–22 GJ/1000 m^3. When processed for the removal of particulates and water, this gas is suitable for combustion in boilers, furnaces turbines, or engines for conversion to steam and/or electricity.

Over the past 20 years, a significant amount of research and development has been conducted on improving the design and performance of LFG systems. A significant amount of this R&D has been funded over the past decade by the Department of Energy, The Gas Research Institute, and private industry which has led to strategies to stimulate bioconversion of MSW to biogas, to improve methods of distributing water and nutrients, and to more effectively design landfills from scratch to provide more efficient gas collection (Bogner, 1990). At present, the technology is developed well enough to attract commercial participants to introduce the technology into the market place. But future R&D will likely produce substantial improvements in the stimulation of bioconversion rates achievable in LFG systems, system control, and gas management, thereby yielding further improvement in the profitability of LFG systems.

These participants includes a good number of architectural and engineering (A&E) firms that market a repertoire of MSW management options to city and county governments. This technology is very well suited to A&E dominance since it involves very little process hardware and since it requires a great deal of engineering design, environmental management and earth work that is the mainstay of the engineering firm business.

There are very few competing technologies available for the extraction of methane from already-in-place MSW residues in landfills. The main competition that occurs in this arena is between the particular approaches each engineering firm uses to provide enhancements to biogas generation and collection. For landfill systems planned and operated from scratch, the principal competing technology for biogas generation comes from the previously discussed technology of separation of recycled plastics and metals followed by above-ground conversion of the organic fraction of MSW to biogas. The advantages and disadvantages of each have been covered in the previous section.

3.4.3 Market Considerations The state of current marketing climate in landfill gas is found in a document put out by Governmental Advisory Associates, Inc. called "Methane Recovery from Landfill Yearbook" (Berenyi and Gould, 1992). This report provides detailed survey information on LFG facilities throughout the United States based on 1991 data. Important facts from the Yearbook that relate to today's LFG market environment are the following:

- There are about 157 landfills in the United States that are producing or plan to produce biogas. Over 80 percent of these are fully operational; the rest are in the planning or construction/shakedown phases.

- Currently, about 64 PJ of biogas is produced each year from 115 existing LFG facilities. Biogas output capacity from planned and existing facilities exceeds 87 PJ per year.

- LFG-to-energy plants in all stages of development are identified in 32 states including the District of Columbia. By region, 38% are cited in the West, 20% are in the South, 26% are in the Northeast, and 17% are located in the Northcentral states.

- The landfill gas industry exhibited slow but steady growth from the late 1970's until the mid-1980's. Since then, new projects have come on-line in double digit rates and almost 60 percent of all working facilities have started operations since 1986.

- Over two-thirds of the LFG facilities generate or plan to generate electricity, while the remaining plants collect and refine medium-Btu gas for sale to a direct user or to a utility.

- The average heating value of the raw LFG generated at the production sites around the country is over 19 GJ/1000 m^3 (490 Btu/scf) which can be upgraded to pipeline quality gas at over 37 GJ/1000 m^3 (970 Btu/scf).

- Over 91 percent of the LFG facilities employ collection wells to remove biogas from their landfills; the remaining facilities use horizontal trenches or trenches and wells in combination.

- The average gas flow rate of LFG facilities was 2,700 GJ/day (2.58 million cubic feet per day) with a range of 42 to 33,600 GJ/day (0.040 to 31.70 million cubic feet per day).

- The average price paid for electricity by utility customers was 6.13 cents/KWH with a range of 2.3 to 10.8 cents/KWH.

- The average capital cost of LFG facilities in 1991 dollars was $4.9 million per facility with a range of $0.105 to 31.2 Million.

- Annual operation and maintenance (O&M) costs averaged $554,000 per facility per year with a range of $2,400 to $4.1 million per facility per year.

- The average royalty paid to landfill owners by LFG facility developers was a little more than 15% of project revenues.

- The majority of LFG facilities (about 84%) were privately financed by their owners.

The largest LFG facility plant in the country is the Puente Hills Energy Recovery from Gas (PERG) Facility located at the Puente Hills Landfill in Whittier, CA and operated by the Los Angeles County Sanitation District (Valenti, 1992). This landfill contains over 41 million Mg of waste in place and receives 65,000 additional Mg every week. In operation for LFG production since 1986, the PERG facility generates 290 m^3/min of landfill gas which is used to fire two steam generators, producing 95,000 Kg of steam per hour at 9.3 MPa (guage) heated to 540 °C. This steam drives a Fuji Electric Co. Ltd. turbine that generates approximately 50 megawatts of electricity (gross) and 46 megawatts net that are sold to Southern California Edison, sufficient electricity to service 100,000 homes (Valenti, 1992).

Environmental considerations have not seriously constrained LFG technology. Operating experiences in California, one of the most stringent states for air pollution regulations, have shown that even LFG to electricity facilities can provide economical energy production benefits while still meeting pertinent air pollution regulations. Stringent local and state regulations, such as those in California, have led landfill power systems to use gas turbines rather than reciprocating engines because the former produce less NO_x. These regulations have even impacted boiler design. The boilers at PERG are oversized to lower the specific heat rate, reducing emissions to meet local air standards.

Principal market drivers for LFG facilities include: 1) greenhouse gas emission control (i.e., methane and carbon dioxide), 2) benefits in reducing water-soluble constituents that pose a groundwater contamination potential in landfills, and, 3) profits that may be realized through electricity generation. The first two drivers have already been discussed in the previous section. Site-specific affecting LFG recovery from landfills and the resulting emissions of greenhouse gases is discussed in a recent EPA report (Campbell et al., 1991).

The last driver is highly dependent on the price that can be obtained for electricity. In the past, landfill methane was tapped for electricity if the local utility needed additional capacity and found it economical to purchase power from that source. The Public Utility Regulatory Policy Act (PURPA), passed in the wake of the first OPEC oil embargo when oil prices soared, required utilities to buy power that was generated from LFG facilities at a price that was profitable to the feneraters, thereby providing revenue to landfill power systems. Under PURPA, utilities must accept all co-generated electricity, pay "fair market value" based on avoided costs, and provide stand-by service at reasonable cost. But "fair market value" is determined on a case-by-case basis and depends upon the local market needs as well as the outcome of negotiations between the entrepreneur, the utility and the pertinent regulatory agencies. Thus, LFG facilities have encountered various negotiated "fair market" prices ranging from less than 3 cents to 8 cents in the United States. Since it typically requires 2 to 2.5 cents to pay for the engines and gas handling systems alone, it is generally recognized that in today's economy revenues of at least 5.5 to 6 cents per KWH are needed to provide an adequate payback for most LFG to electricity facilities. Rigorous present-worth analysis of total facility costs versus all revenue streams is needed to provide a sound business basis for profitable operations.

Overall, LFG is a rapidly growing industry that will benefit in future years from R&D and advances in engineering that will improve productivity and construction cost. Since LFG operations have multiple environmental benefits in terms of groundwater protection, air pollution control and greenhouse gas emissions reduction, the technology is likely to enjoy favorable regulatory treatment. Given these factors, LFG is expected to continue to grow as a good business opportunity for biogas generation.

3.5 Wastewater Treatment

3.5.1 Status of the Technology As seen in table 93, there are a number of commercial processes that use anaerobic bacteria to treat wastewater of various strengths. Nearly 25 years ago, anaerobic digestion was believed to have limitations in not being applicable to wastewater streams more dilute than 1000 ppm total organic carbon since the state-of-the-art of anaerobic digestion was comprised mainly of suspended culture systems and since it was considered essential that the feedstream be high enough in organic concentration to provide adequate microbial cell growth rates (Metcalf and Eddy, 1972). Over the past two decades, the commercial introduction of fixed film reactors (e.g., trickling filter and the fluidized bed reactor) and the granular sludge blanket reactor have made it possible to apply anaerobic digestion to wastewaters with organic concentrations as low as 100 ppm.

3.5.2 Resource Base The application of anaerobic processes to the conversion of organic pollutants in wastewater to biogas is a technology of high potential in the management of wastewater for municipalities and industry, but of low importance in terms of the amounts of biogas that can be realized from this source. Wastewater management in the United States is a big business in both the industrial and municipal sectors. On an average day, over 26 billion liters of municipal sewage are treated in cities across the United States Industrial wastewater volumes are also sizable; the U.S. Department of Commerce estimates that major industrial water users discharge approximately 1100 billion liters of wastewater daily. About two-thirds of this output is generated by industrial cooling operations, about 10% is generated by agricultural operations and about 10% is generated by manufacturing and minerals.

These flows can be used to estimate an ultimate biogas generation potential for the anaerobic wastewater treatment technology (AWTT). Specifically, biogas potential can be calculated from wastewater flows from municipal sewers and from certain types of industries generating nonhazardous wastewaters. Industrial operations generating wastewaters containing nonhazardous organic pollutants include food processing, meat packing, wood and paper, and beverage. This category of industrial wastewater is undoubtedly a minor fraction of the 86 billion liters per day generated by the manufacturing and minerals category of industry; the amount of water from this source probably totals no more than the municipal wastewater daily flow of 26 billion liters per day. Thus, the total of municipal and nonhazardous industrial wastewater flows total approximately 53 billion liters per day. Since considerable infrastructure (i.e., treatment facilities based on aerobic biological processing and physico-chemical treatment) is already in place to treat much of this wastestream, it would be an ambitious undertaking to capture more than 10% of this market for conversion to biogas. If 5 billion liters/day of this water treatment market could be captured for biogas generation, and if the concentration of biodegradable organics in the composite wastewater is about 100 ppm, then the amount of organics that can be accessed for conversion to biogas can be estimated from the following expression:

KG of Organics/yr = Organic Conc (g/l) × Flow (l/d) × 365 (d/yr) × 10^{-3} Kg/g = 100 mg/l × 5 × 10^9 l/d × 365 d/yr × 10^{-6} Kg/mg 1.82 × 10^8 Kg/yr

If it is assumed that organics are removed from wastewater with a 90% efficiency, and that organics in wastewater have methane yield of glucose approximating 440 ml/g (or 0.440 m^3/Kg) where the methane has an energy content of 0.037 GJ/m^3, the biogas equivalent of organics converted in anaerobic digestion processing can be calculated as follows:

Biogas, PJ/yr = WW Organics (Kg/yr) × Yield m^3/Kg × 0.037 GJ/m^3 × 10^{-6} PJ/GJ = 1.82 × 10^8 Kg/yr × 0.440 m^3/Kg × 0.037 GJ/m^3 × 10^{-6} PJ/GJ = 3.0 PJ/yr

3.5.3 Market Considerations The biogas production potential of 3.0 PJ/yr is less than 1% of the biogas generation potential from MSW which was previously discussed. Furthermore, this low level of biogas generation may still be overstated since at the low conbentrations at which anaerobic waste treatment is likely to be applied, the amount of methane solubilized in the water and escaping in the effluent stream can represent methane losses amounting to 25–50% of the total methane produced (Hayes et al. 1990). Based on these considerations, biogas generation from wastewater does not appear to be an attractive investment opportunity if energy production is the prime objective.

This is not to say that anaerobic processing cannot have good business prospects for other reasons—namely for wastewater treatment and site remediation purposes. The wastewater treatment field has experienced steady growth over the past decade due to emerging regulatory pressures and if anaerobic processing can compete with existing treatment methods, one can expect a steady market growth for anaerobic wastewater treatment. Anaerobic processing of wastewater can provide special transformations that are useful in treating complex mixtures of organic pollutants; for example, anaerobic processing can provide dechlorination of chlorinated ethenes (i.e., perchloroethylene and trichloroethylene) that can provide important preprocessing within a treatment train of biological and physicochemical treatment. However, market opportunities for biogas generation purposes alone are not likely to come to fruition for anaerobic wastewater treatment due to the inescapable constraints of low biogas generation potentials from wastewater.

4. Conclusions

Based on the discussions and information presented in this chapter, the following conclusions seem reasonable:

- The major categories of technically feasible biogas technology applications include: 1) Manure conversion via anaerobic digestion, 2) Landfill gas (LFG); 3) Anaerobic bioconversion of community wastes (MSW) in above ground processes; 4) Wastewater treatment; and, 5) Biomass-to-methane systems.

- Over 75% of all manure material is generated on small farms at a rate of less than 3 dry Mg/d (500 cow-equivalent) with a methane generation capacity of less than 25 GJ/day. The collection of this small amount of biogas from tens of thousands of on-farm generators would likely be cost prohibitive, although the relatively few feedlots and poultry operations that produce more than 5 dry Mg/d would represent good sites for commercial-scale biogas production. The cost of producing pipeline-quality methane from manure totals $5/GJ for anaerobic digestion with a throughput of more than 2 Mg/d and $2/GJ for gas cleanup. This total price of $5/GJ cannot compete with current or future gas acquisition prices. Medium-Btu biogas costing $3/GJ, however, would be an attractive, cost-saving replacement fuel for more expensive on-farm energy including electricity, fuel oil, and propane. Farm operations would have to assess the potential of this technology in terms of the economic benefits of on-farm biogas energy use and the fuels and electricity displaced by biogas usage.

- Biomass-to-methane systems do not represent a near-term or mid-term investment opportunity because of the lack of credible pilot experience and due to low natural gas acquisition (wellhead) prices reflecting an abundance of foreseeable supplies for the next 20 years. However, should a future national need arise for supplemental gas, well-developed technologies from biomass production to anaerobic digestion—

verified in small pilot systems and in commercial applications other than biomass (i.e., MSW bioconversion)—are available and few logistical barriers to implementation exist.

- Anaerobic processing for wastewater treatment does not appear to be an attractive technology for biogas generation alone, though significant markets are expanding for industrial wastewater treatment and site remediation purposes.

- Landfill Gas (LFG) is the fastest growing biogas business in the United States today because of multiple market drivers including environmental benefits (e.g., greenhouse gas emissions control) and PURPA-based negotiations. This area will continue to represent good investment opportunities, particularly in areas where electricity can be sold to utilities at a purchase price exceeding $0.06/KWH.

- Anaerobic bioconversion of MSW in aboveground bioprocesses is an emerging technology in Europe and an infant technology in the United States that can provide investment opportunities in the United States if certain economic drivers provide adequate incentives. This application of anaerobic digestion has a large advantage over biomass and manure applications for two reasons. First, biogas generated through the anaerobic digestion of MSW will occur near the city gate and will compete with city gate prices at $34/GJ while biogas from biomass and manure systems is generated in more remote locations and will likely compete with acquisition (well-head) prices that are about $2.00/GJ; the product gas from MSW systems is therefore worth about $1/GJ more than biogas from biomass and manure systems. Secondly, large credits can be taken for waste disposal in MSW systems that cannot be obtained for manure and biomass applications. Because of these advantages, MSW to biogas appears to be one of the most promising new application biogas opportunities for the 1990's.

- In addition to revenues that can be realized from biogas and/or electricity generation, the most important market drivers for MSW biogas systems in the next decade will include: 1) reduction of groundwater pollution potential of MSW; 2) extension of landfill life by a factor of 3 to 5; and, 3) control of greenhouse gas emissions. High solids systems, where engineering problems have been worked out, will present the best potential for profitable enterprises. The biggest barrier to market development in this area is a lack of familiarity and confidence in the technology among municipal and state decision makers due to the low number of pilot and commercial installations in United States today.

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Biological Conversion of Fossil Resources

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1. Introduction

Microorganisms may be used to directly recover or convert fossil resources into valuable consumer products. Our most abundant fossil resource, coal, may be converted into fuels or chemicals by the action of fungi or bacteria, or other biocatalysts derived from such organisms. Microorganisms are also able to biosolubilize coal to produce a water soluble product. This solubilized coal can then be converted to ethanol or methane (CH_4) by reaction with anaerobic bacteria. The components of coal synthesis gas and petroleum fractions may be used as a feedstock in the biological production of organic acids, alcohols, methane or hydrogen (H_2) with anaerobic bacteria. Similarly, natural gas and petroleum fractions may be used as a raw material for the production of methanol or bacterial-derived single cell protein.

Microorganisms may be used in the recovery of oil from oil fields through microbial enhanced oil recovery. In addition, bacteria have been found to be capable of removing oil from tar sands and oil shale, either through the formation of surfactants or by the production of acid which attacks the limestone-kerogen matrix.

In general, microbial processes offer certain important advantages over traditional technology. Yields from biological conversion are quite high, since the microorganism uses only a small fraction of the substrate for energy and growth. Under proper conditions, microbial reactions are quite specific, generally converting a substrate into a single product, with only small quantities of by-products. Microorganisms can often obtain necessary hydrogen from water and thus do not require an external source of hydrogen for conversion. These advantages are offset, somewhat, by slower reaction rates and special reactor considerations, such as sterility and nutrient provision.

This chapter will focus on the technical aspects of the various biocatalytic technologies associated with fossil resource conversion and recovery. In addition, the potential for commercialization of each technology will be discussed, as well as the limitations or problems which may impede or limit commercialization.

2. Coal Conversion Technologies

Coal may be directly or indirectly converted to fuels and chemicals. Direct conversion refers to the microbial attack of solid coal by fungi or bacteria.

Anaerobic bacteria, isolated from natural sources, may then be utilized to convert the solubilized coal to liquid or gaseous fuels. Indirect conversion refers to the biological reaction of coal synthesis gas, a mixture of predominantly carbon monoxide (CO), hydrogen (H_2) and carbon dioxide (CO_2), formed by the oxygen-limited gasification of coal. Anaerobic bacteria grow and utilize syngas components to produce several gaseous and liquid fuels or chemicals. Each of these biological processes offer certain advantages. Direct microbial conversion offers the potential for in situ operation which has the economic potential to be quite attractive. Indirect conversion permits easier mass transfer of the gaseous substrate to the organisms in liquid culture without the added resistance of a solid coal matrix.

2.1 Indirect Coal Conversion

Synthesis gas may be used as a raw material for fuels and chemicals production. Synthesis gas is produced by the gasification of coal, oil, natural gas and biomass in the absence of oxygen. Although the composition of synthesis gas depends upon the gasification process and raw material employed, typical coal-derived synthesis gas contains 40–65% CO, 25–35% H_2 and 1–20% CO_2 (Coffin, 1984). Also present are lesser quantities of CH_4 and sulfur gases such as hydrogen sulfide (H_2S) and carbonyl sulfide (COS). Bacteria have been shown to produce CH_4, H_2, acids and alcohols from CO, CO_2 and H_2 in synthesis gas, and have also been shown to be quite tolerant of the sulfur gases H_2S and COS in their typical concentrations of 1–2% (Vega et al., 1990). Other organisms, most notably Thiobacillus denitrificans and Chlorobium thiosulfatophilum, are able to convert H_2S and COS to elemental sulfur and sulfate.

2.1.1 Alcohol Production In addition to acetic acid, the bacterium Clostridium Ijungdahlii produces ethanol from CO, CO_2 and H_2 by the equations (Barik et al., 1988; Vega et al., 1989):

$$6\,CO + 3\,H_2O \rightarrow \underset{\text{(ethanol)}}{C_2H_5OH} + 4\,CO_2 \qquad (1)$$

$$2\,CO_2 + 6\,H_2 \rightarrow C_2H_5OH + 3\,H_2O \qquad (2)$$

Although the "wild" strain produces acetic acid preferentially to ethanol (product ratio 20:1), studies at reduced pH and with a defined nutrient medium have resulted in product streams containing almost entirely ethanol (Phillips et al., 1993). As is shown in figure 74, experiments carried out in a continuous stirred tank reactor (CSTR) with cell recycle at a 20 min gas retention time resulted in ethanol concentrations of 47 g/L, with only small amounts of acetic acid produced as a by-product. No other liquid by-products were produced. The yields of ethanol and acetic acid were stoichiometric as presented in eqs (1) and (2).

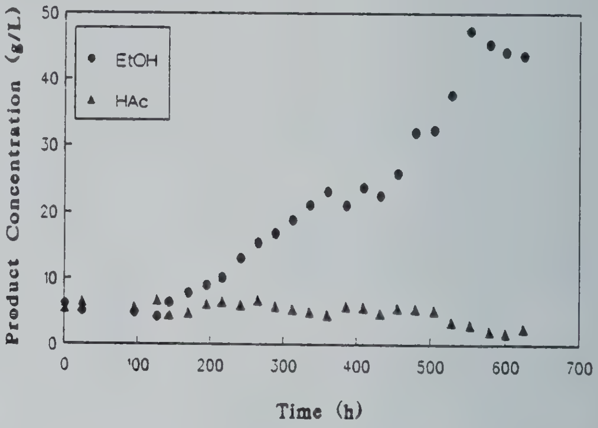

Fig. 74. Production of ethanol and acetate by C. Ijungdahlii from synthesis gas in the CSTR with cell recycle.

The anaerobic bacterium Clostridium acetobutylicum has been shown to produce small amounts of butanol, along with lesser amounts of ethanol and acetone in converting butyrate produced from CO by B. methylotrophicum (Grethlein, et al., 1990). Butyrate conversion occurs when using hydrogen or small amounts of glucose to supply the reducing equivalents.

Continuous reactor studies in a variety of reactors have been performed with C. Ijungdahlii, including a trickle bed reactor and a high pressure reactor (Clausen and Gaddy, 1992). Nevertheless, in comparing rates of ethanol production, the CSTR with cell recycle appears to be the best reactor for ethanol production.

2.1.2 Hydrogen Production Hydrogen production traditionally occurs by the catalytic water gas shift reaction

$$CO + H_2O \rightarrow CO_2 + H_2 \qquad (3)$$

where CO and steam are reacted to form CO_2 and H_2 in the presence of a heterogeneous mixture of metal catalysts at elevated temperatures (McCullough et al., 1982). Certain bacteria are also able to catalyze the reaction of eq (3), at ordinary temperatures of 25–50 °C with fast rates and high yields.

As is shown in table 108, three organisms are known to carry out the reaction of eq (3). R. gelatinosa grows very slowly on CO in the dark and thus has little commercial potential (Uffen, 1986). R. rubrum grows on a variety of organic carbon sources in the presence of tungsten light (Dashekvicz and Uffen, 1979). Light is not required by R. rubrum, however, for the biocatalysis of eq (3). Engineering resources, Inc. recently isolated a thermophilic (optimum temperature of 50 °C) bacterium (ERIH2) which does not require light for growth and grows on organic carbon sources such as glucose. Of these three organisms, ERIH2 has the most commercial potential, producing stoichiometric yields of H_2 with 90% CO conversions at an 8 min gas retention time. Both R. rubrum and ERIH2 have been utilized in bench scale fermentation processes involving continuous bioreactors (see Sec. 5.).

Table 108. Bacteria capable of biological water gas shift

Bacteria	Optimum Temperature (°C)	Comments	Yield of H_2 from CO & H_2O in Eqn. (3)
Rhodopseudomonas gelatinosa	35-37	slow growth on CO	low
Rhodospirillum rubrum	30	requires light for growth; no growth on CO	0.87
ERIH2	50	no growth on CO	1.00

Klasson et al. (1993) studied R. rubrum for its capability of converting CO and water to CO_2 and H_2 by the water gas shift reaction in batch culture. The specific CO uptake rates were determined and the effects of elevated CO pressures modeled. The results indicate that the specific uptake rate may be related to dissolved CO tension, with substrate inhibition occurring according to an Andrews modification of the Monod equation:

$$q = \frac{0.055\,P_L^{*}}{0.45 + P_L^{*} + \left(P_L^{*}\right)^2/0.106} \tag{4}$$

where q = specific CO uptake rate, mol $g^{-1}h^{-1}$ and P_L^{*} = dissolved CO tension, atm. Similar results were obtained in the CSTR. The yield of H_2 from CO and H_2O by R. rubrum was 0.87 mol mol^{-1}, or 87% of theoretical. In addition, growth on acetate was studied at light intensities ranging from 100–800 lux in batch culture. Modeling results indicate that growth is dependent upon light intensity according to a Monod type relationship:

$$\mu = \frac{0.052\ Io}{140 + Io} \tag{5}$$

where μ = specific growth rate, h^{-1} and Io = initial light intensity, lux. The cell yields on acetate and ammonia were 0.42 g g^{-1} and 13 g g^{-1}, respectively.

2.1.3 Organic Acid Production Acetic and butyric acids may be produced from CO and CO_2/H_2 by the equations:

$$\underset{\text{(acetic acid)}}{4\,CO + 2\,H_2O \rightarrow CH_3COOH + 2\,CO_2} \tag{6}$$

$$2\,CO_2 + 4\,H_2 \rightarrow CH_3COOH + 2\,H_2O \tag{7}$$

$$\begin{aligned} 4\,CO \rightarrow\ & 2.09\,CO_2 + 0.63\,CH_3COOH + \\ & 0.043\,\underset{\text{(butyric acid)}}{C_3H_7COOH} + 0.027\,\underset{\text{(ethanol)}}{C_2H_5OH} \\ & + 0.43 \text{ cell mass} \end{aligned} \tag{8}$$

A large number of bacteria are capable of carrying out the reactions of eqs (6) and/or (7) as is listed in table 109 (Diekert and Thauer, 1978; Genthner and Bryant, 1982; Lynd et al., 1982; Lorowitz and Bryant, 1984). Of these organisms, A. kivui and Strain ERI2 from Engineering Resources have the highest rates of substrate (CO, CO_2/H_2) utilization (see table 109).

Table 109. Performance summary for various acetogenic bacteria

Direct Route	Max. Co. Consumption Rate, mmol/g hr	Max. H_2 Consumption Rate, mmol/g hr		Ability to Consume CO and H_2 Simultaneously
		Waste Gas	H_2/CO_2	
P. productus	19.0	3.6	3.7	No
E. limosum	18.0	5.0	19.1	No
A. noterae	17.0	3.0	9.1	No
C. aceticum	18.9	0.0	0.0	No
C. thermoaceticum	7.3	2.9	8.1	No
S. sphaeroides	0.0	0.0	34.0	No
A. woodii	6.8	6.7	16.1	Yes
A. kivui	27.5	49.2	60.0	Yes
Indirect Route				
R. rubrum (ATCC 9791)	13.1	--	--	No
R. rubrum (ATCC 25903)	8.7	--	--	No
R. gelatinosa	0.0	--	--	No

Researchers at Michigan Biotechnology Institute (Worden et al., 1989) have shown that the anaerobic bacterium Butyribacterium methylotrophicum is capable of converting CO to acetic acid, butyric acid and ethanol, with acetate being the major product. Growth on CO_2/H_2 produces acetate only. The ratio of butyric acid formation to acetic acid formation by B. methylotrophicum varies significantly with pH. The empirical stoichiometric equation at pH 5.5 is:

$$4\ CO \rightarrow 2.18\ CO_2 + 0.4\ CH_3COOH + 0.154\ C_3H_7COOH + 0.04\ \text{cells} \qquad (9)$$

The acetogenic bacteria P. productus, A. kivui and ERI2 have been successfully used in bench scale fermentation processes involving continuous bioreactors (see Sec. 5.). Acetic acid concentrations using A. kivui or ERI2 in stirred tank reactions (CSTRs) with cell recycle at a 3 min gas retention time are approximately 20 g/L.

2.1.4 Methane Production Methanogens are well known to convert CO_2/H_2 and acetate to methane by the equations (Jones et al., 1987; Huser et al., 1982):

$$CO_2 + 4\ H_2 \rightarrow CH_4 + 2\ H_2O \qquad (10)$$

$$CH_3COOH \rightarrow CH_4 + CO_2 \qquad (11)$$

Table 110 lists some of the more common methanogens and the substrates they utilize. Only one bacterium, Methanobacterium thermoautotrophicum, was found to be capable of converting CO to CH_4, and it was later found that this strain was in reality a mixed culture (Daniels et al., 1977).

Table 110. Common methanogens and their substrates

Bacterium	Substrate
Methanosarcina barkeri	acetate, CO_2/H_2
Methanobacterium formicicum	CO_2/H_2
Methanothrix soehngenii	acetate
Methanospirillum hungatii	CO_2/H_2
Methanobacterium mobilis	CO_2/H_2
Methanobacterium ruminantium	CO_2/H_2
Methanococcus vannielii	CO_2/H_2
Methanosarcina methanica	acetate

In converting CO_2 and H_2 in synthesis gas to CH_4, it is seen that, because of the composition of synthesis gas, the gas is deficient in H_2 to allow complete utilization of CO_2. Thus, in order to most efficiently utilize the components of syngas, organisms are combined either as a series of pure cultures in separate reactors or as co-cultures in a single reaction vessel. Two systems are possible: (a) CO and water conversion by H_2-producing bacteria:

$$CO + H_2O \rightarrow CO_2 + H_2 \qquad (3)$$

followed by conversion of CO_2 and H_2 by methanogens:

$$CO_2 + 4\ H_2 \rightarrow CH_4 + 2\ H_2O \qquad (10)$$

or (b) CO and CO_2/H_2 conversion to acetate by acetogenic bacteria:

$$4\ CO + 2\ H_2O \rightarrow CH_3COOH + 2\ CO_2 \qquad (6)$$

and

$$2\ CO_2 + 4\ H_2 \rightarrow CH_3COOH + 2\ H_2O \qquad (7)$$

followed by conversion of acetate to CH_4 by methanogens:

$$CH_3COOH \rightarrow CH_4 + CO_2 \qquad (11)$$

The net reaction for both of these routes assuming a H_2 deficient system is:

$$4\ CO + 2\ H_2O \rightarrow CH_4 + 3\ CO_2 \qquad (12)$$

Thus, a product gas of 25 percent CH_4 and 75 percent CO_2 results for this system. The composition of the product stream will vary depending upon the composition of the syngas stream.

Researchers at the University of Arkansas have investigated the feasibility of both bacterial systems for CH_4 production (Barik et al., 1988). Separate pure cultures and co-culturing systems were employed. Although each of the systems are limited by the slow growth of methanogens, the system utilizing H_2-producing bacteria and methanogens was found to be more stable and thus superior. In fact, a bacterial system employing R. rubrum, M. barkeri and M. formicicum was effectively utilized in CSTR and trickle bed reactor systems, producing stoichiometric quantities of methane and CO_2 from syngas (Kimmel et al., 1991).

Figures 75–78 show CO and H_2 conversions to methane in both 2-in and 6-in diameter trickle bed reactors using the tri-culture. Conversions to CH_4 from CO and H_2 were stoichiometric.

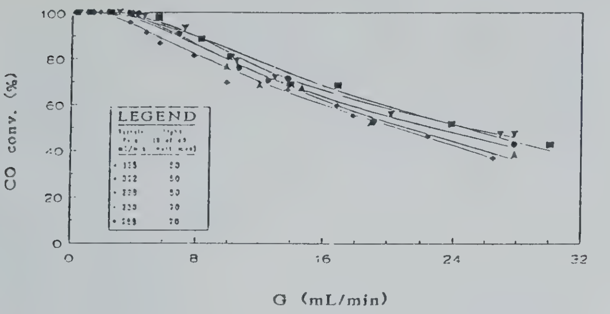

Fig. 75. Carbon monoxide conversion as a function of the average gas flow rate for the two-inch trickle-bed reactor.

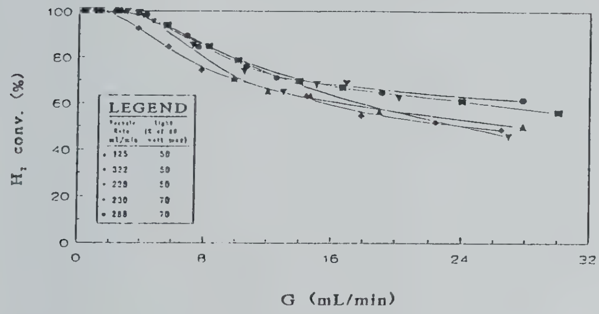

Fig 76. Hydrogen conversion as a function of the average gas flow rate for the two-inch trickle-bed reactor.

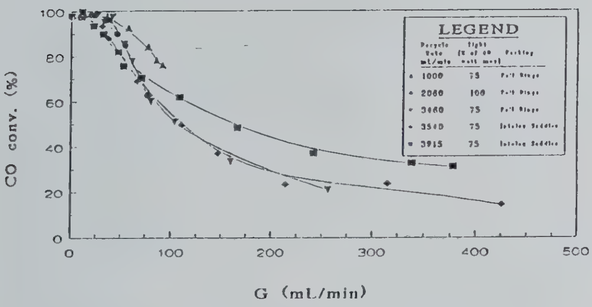

Fig 77. Carbon monoxide conversion as a function of the average gas flow rate for the six-inch trickle-bed reactor.

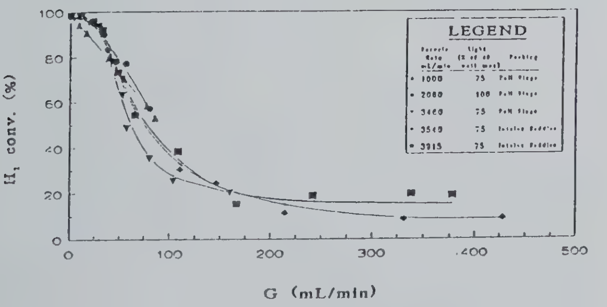

Fig. 78. Hydrogen conversion as a function of the average gas flow rate for the six-inch trickle-bed reactor.

2.1.5 Economic Considerations The economic potential of the various indirect coal conversion technologies has been evaluated in order to prepare for demonstration and commercialization. The technology for ethanol, hydrogen and organic and production has been demonstrated in bench scale units and is ready for further demonstration in pilot units.

A process for the production of either ethanol or acetic acid from synthesis gas would be quite simple. Syngas would be fed to a biological reactor where bacteria convert CO, CO_2 and H_2 to the desired product. Cell recycle is used to maximize the concentration of cells inside the reactor, and high agitation rates are utilized in stirred tank reactors to maximize gas-liquid mass transfer. Following product formation, the ethanol or acetic acid is separated from dilute aqueous solution by employing solvent extraction followed by distillation.

Economic projections for a 20 million gallon ethanol production facility would require a capital investment of $8 million excluding the cost of the gasifier. Operating costs for a coal to ethanol facility including utilities, labor, overhead, supplies and chemicals, depreciation, taxes and insurance and maintenance total $7.4 million. It is assumed in this analysis that the synthesis gas costs $6 per million Btu. With a revenue of $25 million per year ($1.25/gallon), the investment would be returned in 2.3 years.

Similar economics result for acetic acid production from syngas. For a 100 million lb/yr facility, a capital cost of $10.8 million is required excluding gasification. The operating costs including $6/MMBtu for syngas, total $10.6 million. The payout for this process using an acetic acid value of $0.18 per pound is 1.6 yr.

A biological process for H_2 production is similar to the chemical production processes except that either a stirred tank reactor or a column reactor may be used, and H_2 purification is different from ethanol or acetic acid recovery. In processing 500 tons/day of coal to produce H_2, a capital investment, including the gasifier and H_2 purification, is $19.9 million. This process is able to produce 21.6 million ft^3 of H_2 per day. The operating costs for the facility total $8.6 million/yr, including coal at $20 per ton. The revenue from H_2 production at $1.84/MSCF is $14.0 million/yr and the process returns about 30 percent per year.

2.1.6 Limitations of This Technology Biological synthesis gas conversion is a relatively mature technology. In fact, the conversion of syngas components to ethanol, H_2, acetic acid and CH_4 has been sufficiently developed in the engineering laboratory to permit demonstration of the technology in pilot facilities. Following pilot scale demonstration, where all of the unit operations involved in fermentation and product recovery are linked and demonstrated, commercial scale facilities can be built.

Several questions arise when considering the use of biotechnology for commercial syngas conversion to commodity chemicals or fuels:

1. Can inexpensive sources of syngas or other similar gas be obtained?
2. Can bacterial reactor systems be run continuously for extended periods of time with minimal shutdown time?
3. Can commercial product recovery technology be successfully linked to bioreactor systems?
4. What will be the market impact for these products produced by biotechnology?

The answers to these important questions are process specific. Because of large reserves of natural gas, methane production from syngas appears to be uneconomical at this time. On the other hand, large quantities of H_2 and ethanol are expected to be required for fuel and fuel upgrading.

2.2 Direct Conversion of Coal

2.2.1 Biosolubilization Tremendous potential exists for the direct in situ microbial conversion of coal to liquid fuels. Conceptually, organisms and medium would merely be injected into a fractured coal seam where, over time, the organisms would convert the coal to liquid products. The period of time for conversion could be many months since essentially no labor is required for the conceptualized process. Once formed, the liquid product would be pumped from the formation and harvested for product recovery and ultimate sale.

2.2.1.1 Brief History Aerobic organisms, either fungi or bacteria, are used to produce a black water-soluble compound of high average molecular weight from low-rank coals (Dahlberg, 1986; Wilson et al., 1986; Scott et al., 1986). The temperatures for the conversions are typically 25–37 °C. A wide variety of organisms have been shown to be capable of this conversion (Cohen and Gabriele, 1982; Scott et al., 1986; Cohen, 1986; Wilson et al., 1986; Strandberg and Lewis, 1986) as is shown in table 111. The basis for this conversion is the similarity between lignin, a constituent of lignocellulosic materials such as wood, and lignite, a low-rank coal. In fact, the earliest reported fungus capable of biosolubilizing lignite was the white-rot fungus Trametes versicolor.

Table 111. Microorganisms known to biosolubilize lignite

Trametes versicolor
Streptomuces setonii
Streptomyces viridosporus
Aspergillus sp.
Candida sp.
Geosmithia sp.
Paecilomyces sp.
Steptomyces sp.
Penicillium sp.

The biosolubilization of low rank coals generally works best on pretreated or highly oxidized coals using fungi or bacteria grown in the presence of a rich nutrient medium (Scott et al., 1986). Pretreatment with 6N nitric acid, ozone or even air oxidizes the coal, thereby making the coal more susceptible to microbial attack (Strandberg et al., 1986; 1987). The naturally oxidized coal, Leonardite, is easily biosolubilized without pretreatment. The susceptibility of attack is also obviously increased by employing small particle sizes. The grinding of Leonardite to 60 mesh insures complete biosolubilization in a relatively short period of time.

The biosolubilization of coal can occur both in surface culture or submerged culture. Surface culture solubilization occurs after first growing a mat of fungi on an agar of Sarbouraud medium. Less expensive media have been employed in a limited number of cases. Small coal particles brought into contact with this fungal mat will form droplets of solubilized coal.

The submerged culture technique involves first producing a culture broth from the fungi or bacteria of table 111. Pretreated or oxidized coal is then contacted with the medium, usually in a stirred tank reaction vessel (submerged culture), where the conversion to "liquefied coal" takes place.

The liquefied coal produced biologically is a mixture of water soluble, polar organic compounds with relatively high molecular weights. Efforts aimed at quantifying the composition of the bioextract have been limited by the low volatility of the components. It is clear, however, that the product is a mixture of highly polar, water soluble, aromatic compounds with molecular weights in the range of 30,000–300,000 (Wilson et al., 1986; Scott et al., 1986). Elemental analysis shows an increase in carbon content and a decrease in hydrogen content of the bioextract in comparison to coal. There is also a decrease in the methylene functionality in comparison to coal, and there are primary amines and carbonyl functionalities in the bioextract. Also present in the bioextract are polycondensed aromatic ring (structures with any hydroxyl groups.

Partial solubilization of untreated lignite coals has been achieved with less expensive media (Clausen et al., 1991). It has been shown that untreated Arkansas lignite can be 35 percent solubilized with extract from a fungus isolated from an Arkansas lignite outcrop in submerged culture (see fig. 79). The bioextract was prepared from less expensive nutrient medium utilizing cellulose sources.

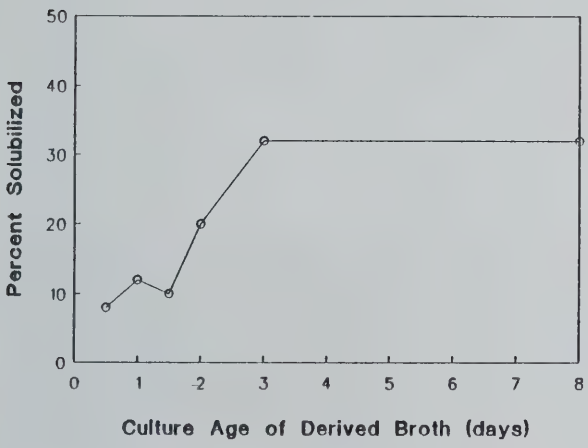

Fig. 79. Solubilization of untreated Arkansas lignite with LSC extract.

There is significant disagreement on the mechanism of biosolubilization. Proposed mechanisms include simple acid/base chemistry, enzymatic conversion and the formation of chelating agents (Scott et al., 1986; Dahlberg, 1986; Wilson et al., 1986). The mechanism of chelating agents being at least partially responsible for biosolubilization is receiving more widespread acceptance. There is little evidence showing that higher rank coals can be biosolubilized. However, there is an indication that microbial and enzymatic interactions do occur.

2.2.2 Conversion of Biosolubilized Coal to Liquid Fuels and Chemicals There is also evidence showing that biosolubilized coal can be converted to organic acids, alcohols and lower molecular weight hydrocarbons by the action of organisms isolated from natural sources (Clausen et al., 1991). The biosolubilized coal should also be more amenable to attack by organisms for the removal of organic sulfur and other heteroatom compounds. Studies at the University of Arkansas showed that a culture isolated from sheep rumen was able to produce up to 3.5 g/L acetate and 3.4 g/L ethanol from relatively low concentrations of solubilized coal in mineral medium (see data of table 112). Evidence was also shown in other experiments that the molecular weight of the biosolubilized coal had been reduced after inoculation with cultures isolated from animal rumen and sewage sludge.

Table 112. Alcohols and acids production from solubilized lignites

Lignite Concentration (percent)	Product Concentration (g/L)			
	ETOH	1-PrOH	HAc	pH
3	0.0469	------	0.4572	8.0
33	3.3616	0.2915	3.4647	5.5

2.2.3 Direct Conversion of Coal to Methane Organisms have been isolated from natural sources that have been shown to directly convert high-rank coal to methane in mineral medium. Studies carried out at Arctech (Barik et al., 1990) have shown that a significant fraction of lignite and subbituminous coals could be converted to methane using organisms isolated from the gut of coal-fed termites. However, since yeast extract was present in the medium, it is quite possible that the yeast extract could have been responsible for a majority of methane produced. Studies presently being carried out at the University of Arkansas have shown that small amounts of methane can be produced from bituminous and sub-bituminous coals, even without yeast extract present in the medium (Johnson et al., 1993). Table 113 presents a summary of this data. The bacterial isolates in these latter studies were obtained from natural sources having contact with sewage sludge or sediment and coal or hydrocarbons over a number of years. Both of these studies require several weeks of incubation for the accumulation of methane and thus point toward the need for a significant amount of development prior to commercialization.

2.2.4 Limitation of This Technology Direct coal bioconversion has been studied in research laboratories for the past 10 years. A significant research and development program will be necessary to demonstrate and commercialize this technology. These conversion technologies employ dilute solutions, either in coal concentration or solubilized

Table 113. Average methane production from various hard coals (no yeast extract present)

	Average* Maximum Production (Volume %)							
	pH 5				pH 7			
Inoculum	P	H	W	Control (no coal)	P	H	W	Control (no coal)
1	0.04	0.08	0.08	0	0	0.13	0.09	0
2	2.16	3.44	0.42	1.54	2.04	1.07	2.69	1.19
3	2.70	5.33	5.49	3.30	3.73	3.41	2.86	1.41
4	0.05	0.14	0.52	0.06	0.08	0	0.15	0
5	3.30	3.14	1.39	3.04	2.88	0.67	3.37	1.69

* - Average of two samples
P - Pittsburgh Seam A
H - Hartshorne
W - Wyodak

coal concentration, which will inhibit commercialization. Biosolubilization processes suffer from economic limitations due to the cost of the medium, the need for pretreatment and the requirement of relatively long fermentation times. The conversion of the biosolubilized product will require a significant amount of culture development to increase product concentrations and decrease fermentation times. Cultures must be developed that solubilize untreated coal and that grow on cheap nutrient sources. Finally, the direct conversion of coal to methane will require a significant amount of development once cultures have been shown to be viable for the production of methane in minimal media.

3. Natural Gas Conversion Technologies

Large reserves of natural gas have been found in this country over the past few years; consequently, uses for methane as a feedstock have been considered. In the presence of aerobic bacteria called methylotrophs (see table 114), methane may be reacted with oxygen (or air) to produce methanol or SCP. The reaction sequence for this conversion is shown in eq (13) (Dalton and Leak, 1985).

$$CH_4 \xrightarrow{O_2} \underset{\text{Methanol}}{CH_3OH} \rightarrow \underset{\text{formaldehyde}}{HCHO} \rightarrow \underset{\text{formate}}{HCOOH} \rightarrow \underset{\text{cells}}{CO_2} \quad (13)$$

As is noted in eq (13), methanol is actually an intermediate in the reaction sequence. The final product of the bacterial conversion is CO_2 and cells (a source of bacterial SCP). In producing either of these products from CH_4 and O_2, the concentrations of CH_4 and O_2 must always be such they do not form a readily explosive mixture.

Table 114. Methylotrophs for methane conversion to methanol or SCP

Methylobacterium sp.
Methylococcus capsulatus
Methylosinus trichosporium
Isolate G1 (Engineering Resources)
Isolate D2 (Engineering Resources)
Isolate FIL (Engineering Resources)

3.1 Methanol Production

The production of methanol from methane and oxygen depends upon interrupting the pathway to allow accumulation of the intermediate. Several techniques have been successfully employed to enhance methanol production, including the addition of ethylene diamine tetracetic acid (EDTA), $CuSO_4$, and phosphate.

Figure 80 shows the effect of adding EDTA and Cu^{2+} on methanol production by Methylosinus trichosporium in batch culture. A maximum methanol concentration of 11 mmole/L (nearly 0.7 g/L) was attained with the addition of 6 mM EDTA and 1mM Cu^{2+}.

When employing the methanotrophs M. trichosporium or Isolate FIL in combination with EDTA and $CuSO_4$ addition to the medium, the methanol concentration obtained from a batch reactor with continuous gas flow was 1.5 Mg/L. A significant research effort thus needs to be undertaken to increase product concentration to establish the commercial feasibility of methanol production from methane.

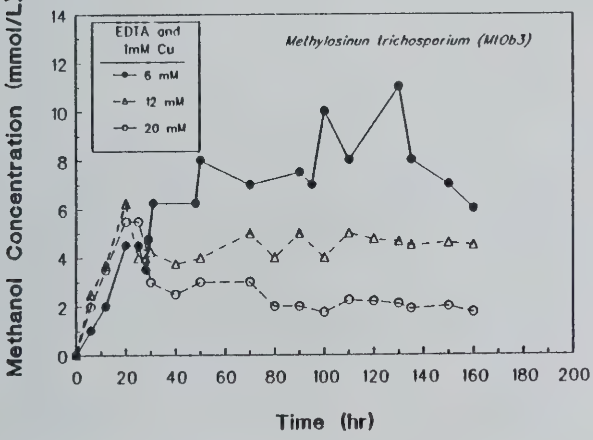

Fig. 80. Effect of EDTA on methanol production with Cu^{2+}.

3.2 SCP Production

Since CO_2 and cells are the ultimate products of CH_4 utilization by methanotrophs, the technology for SCP production should indeed be more advanced. In fact, several commercial ventures have attempted to utilize this technology. These ventures were not successful due to process economics and the problems associated with feeding bacterial protein to animals. Developments in this area are necessary to insure the commercial success of this well developed technology.

Research at Engineering Resources has resulted in the isolation of a bacterium which is able to rapidly produce SCP from CH_4 and O_2. The bacterium has been used successfully in continuous SCP production studies. Field tests are required to determine the viability of this technology as an animal feed.

3.3 Economic Considerations

A process for the production of either methanol or SCP from methane is quite simple. Methane and air are fed to a biological reactor where the conversion to either methanol or SCP takes place. If methanol is the desired product, extractive reaction is necessary to remove the toxic product as it is produced. Product recovery is by distillation if methanol is the final product, and product recovery is by centrifugation and drying if SCP is desired.

In processing 10 million SCF/day of methane to produce methanol, a capital investment of \$11.5 million is required. Conversely, if SCP is produced, the capital investment increases to \$12.4 million. The operating costs for methanol production total \$3.7 million/yr, and yield a payout of 3.4 years if methanol sells for \$0.40 per gal. The operating costs for SCP production total \$13.5 million/yr, and yield a payout of 0.6 years if SCP sells for \$240/ton.

3.4 Limitations of This Technology

As was mentioned previously, the limitation of the methanol production technology is the low concentrations of product formed, which make product recovery difficult. If this problem can be sufficiently addressed, the commercialization of the technology is assured. The major problem impeding SCP development from CH_4/O_2 is the lack of suitability of bacterial protein or an animal feed. Both of these problems are currently being addressed in laboratory development studies.

4. Oil Conversion Technologies

Domestic crude oil production in the United States continues to decline and imports total about 50 percent of the oil requirements primarily for transportation fuels. Primary and secondary oil recovery processes leave about two-thirds of the crude oil in the reservoir. It is estimated that about 350 billion barrels of oil remain in discovered reservoirs in the United States that cannot be recovered by available technology (Knapp, 1985). This 50 year supply (at current usage level) represents a significant resource base for enhanced oil recovery (EOR) techniques.

Oil shale and tar sands deposits occur throughout the world, including the continents of Africa, Asia, Australia, Europe, North America and South America. The United States Geological Survey has estimated a total worldwide recoverable resource of about 3100 billion barrels of oil, contained in oil shales that would yield more than 10 gallons of oil per ton (Ball, 1982; Yen and Chilingarian, 1976). This resource is 1.5 times greater than the worldwide petroleum reserves. The most extensive United States continental deposits of oil shale are the Devonian—Mississippian shales of the eastern states. However, the richest U.S. deposits are in the Green River formation (Eocence) of Colorado, Utah, and Wyoming. These deposits contain 80 billion barrels of recoverable oil, or a 30-year supply of petroleum for the nation. In addition, the United States has 36 billion barrels of oil equivalent as tar sands (Koch, 1982).

4.1 Microbially Enhanced Oil Recovery

EOR techniques usually involve injecting a foreign agent (chemical, heat, microorganism) into the reservoir rock to dislodge, dissolve or otherwise mobilize the oil so that it can be driven to the surface. Each EOR method utilizes one or more of the following recovery mechanisms: (1) re-pressuring the reservoir, (2) mobilizing the oil by reducing the oil viscosity, (3) lowering the interfacial tension of the residual oil trapped in the rock pores by capillary forces, (4) causing the trapped residual oil to swell, thereby creating less absolute residual oil, (5) injecting mobility control polymers to create uniform flooding fronts, thereby creating high sweep efficiencies, or (6) initiating chemical reactions or injecting chemicals that cause the formation of intermediate hydrocarbon solvent banks which dissolve and mobilize the trapped oil. The chemicals and fluids injected into the reservoir should be available in large supply at a reasonable cost and be easily transportable to the field location. These chemicals must be compatible with the reservoir rock and fluids and must remain stable under high shear injection and reservoir conditions of temperature, pressure and salinity.

Microbial enhanced oil recovery (MEOR) involves the use of microorganisms and their metabolic products to stimulate the production of oil from reservoirs of marginal productivity. There are three general approaches (Finnerty and Singer, 1983):

1. Stimulation of the microflora that exists within the reservoir by the injection of requisite nutrients.
2. Injection of specialized microorganisms that produce bioproducts effective in increased oil production.
3. Production of specific bioproducts in large volume fermenters and their subsequent use as chemically enhanced oil recovery agents.

Oil reservoirs are not sterile and aerobes and anaerobes have been isolated up to 10,000 ft depths (Finnerty and Singer, 1983). The microflora are diverse and these organisms are capable of metabolizing hydrocarbons in crude oil. However, the growth and population is limited by other factors such as nutrients, oxygen, and temperature. Therefore, the growth of these indigenous organisms can be stimulated by injecting the limiting factor, such as oxygen or nutrients. These organisms would then enhance oil production by producing surfactants or gases and chemicals that would mobilize oil. Such in situ stimulation can result, however, in overgrowth and pluggage or souring of the crude by production of H_2S by sulfate reducing bacteria (Davis, 1957; McGill et al., 1981). Aerobic microorganisms from reservoirs will be candidates for production of BSP from crude oil in this study.

Microorganisms may also be injected into reservoirs to perform useful functions, such as biosurfactant and biopolymer (BSP) production, gas production, plugging high permeability zones, or bioleaching of rock matrices (Yen et al., 1982; Jenneman et al., 1982). The genera that have been used include Pseudomonas, Escherichia, Arthrobacter, Mycobacteriuim, Micrococcus, Peptococcus, Bacillus, and Clostridium. Fermentable carbohydrates are usually injected with the bacteria and costs can be high. The process is applicable only to low temperature, low salinity ($<100{,}000$ ppm) reservoirs. Major problems are encountered in dispersion of the organisms throughout the reservoirs of low permeability. Several field tests have been conducted around the world with varying results (Ivanov and Belyaev, 1982; Dostalek and Spurny, 1957; Jaranyi et al., 1963; Kuznetsov et al., 1962; Karaskieviecz, 1963; Yarbrough, 1982). A review of these 200 tests has shown that oil production was stimulated in several reservoirs by as much as 300 percent (Hitzman, 1982; Finnerty and Singer, 1983).

The above-ground production of bioproducts as specialty chemicals for application in CEOR represents realistic near- to mid-term technology (Finnerty and Singer, 1983). Microorganisms are capable of synthesizing metabolic byproducts, such as polymers and surfactants, from crude oil, hydrocarbon gases, and a variety of non-hydrocarbon substrates, such as simple carbohydrates, alcohols and acids. These by products are formed either as the result of aerobic or anaerobic metabolism, with the specific microorganism dictating the type of growth conditions necessary for optimal byproduct production. It is important to recognize that the technology supporting large scale growth of microorganisms and recovery of metabolic products is technically advanced, posing no serious problems as to the production of CEOR agents.

Microorganisms produce biopolymers and biosurfactants for various metabolic purposes, such as substrate assimilation. A variety of biopolymers have been produced and tested for the CEOR. These biopolymers are polysaccharides in structure and are listed in table 115. Xanthan gums represent the most important group of biopolymers studied for CEOR.

Table 115. Biopolymers for CEOR applications

Biopolymer	Microorganism
Alginate	*Azotobacter vinelandii*
Xanthan Gum	*Xanthomonas campestris*
Zanflo	*Erwinia tahitica*
PS-7	*Azotobacter indicus*
Curdlan	*Alcaligenes faecalis*
Dextran	*Leuconostoc mesenteroides*
Pullulan	*Aureobasidium pullulans*
Emulsan	*Acinetobacter calcoaceticus*

The most commonly produced biosurfactants are glycolipids, usually a mono- oar di-saccharide attached to a fatty acid. More complex biosurfactants, such as lipopeptides, lipoproteins and lipoheteropolysaccharides have also been isolated. Table 116 lists the biosurfactants and the microbial source. The following sections describe the microbial production of these BSP.

Emulsan is a high molecular weight (10^6), water soluble extracellular biomulsifier, produced by Acinetobacter calcoaceticus. This polymer is a lipoheteropolysaccharide of high molecular weight. The carbohydrate backbone consists of major amounts of D-galactosamine and aminouronic acid with fatty acids of carbon length from C10-C18 attached to nitrogen and oxygen atoms of the sugar backbone (Gutnick et al., 1982). This surfactant forms stable oil-in-water emulsions in which Emulsan concentrates at the oil-water interface. Emulsan has both polysaccharides (polymeric) and polyanionic (surfactant) linkages and may be classified as a BSP.

Table 116. Biosurfactants of microbial origin

Biosurfactants	Microorganisms
Fatty Acids, mono-, diglycerides	*Acinetobacter species*
Emulsan	*A. calcoaceticus*
Trehalose dimycolates	*Rhodococcus erythropolis*
Neutral lipids	*Arthrobacter paraffins*
Corynemycolic acids	*Corynebacterium lepus*
Rhamno-glycolipid	*Candida petrophilum*
Polysaccharide-fatty acid complex	*C. tropicalis*
Sophorolipids	*Torulopsis bombicola*

Xanthan gum is the first microbial polysaccharide of commercial significance and is used in food, industrial and oil field applications. Xanthan gum is produced from the bacterium Xanthomonas campestris (Walker and Gallegly, 1951). The properties of this gum are high viscosity at low concentration and low shear rates; stability to variations of temperature, pH, shear, enzyme degradation; and compatibility with salts over a wide range.

S-130 is a polysaccharide produced by Alcaligenes species (ATCC 31555) in an aerobic submerged fermentation. S-130 produces a high viscosity at low concentrations and low shear rates and, as a result, has good suspending properties. It has excellent solubility in sea water or brine and is compatible with high concentrations of divalent cations at pH values up to 12. The viscosity of S-130 is stable for long periods at high temperature. The significant viscosity stability, tolerance to salinity and broad pH range make this polymer a good candidate for CEOR.

Scleroglucan is produced by different Sclerotium species. The polymers differ in molecular weight and in number and length of side chains, depending on the species. Schleroglulcan contains B-D-glucopyranosyl residues. This polymer readily dissolves in water to give pseudoplastic solutions having a high tolerance to a broad range of temperature, pH, and salt concentration, which makes it an excellent candidate for CEOR.

PS-7 gum is an extracellular polysaccharide, produced by Beijerickia indica var. myxogenes (Kang and McNeely, 1977). This biopolymer contains glucose, rhamnose, glucuronic acid, and O-acetyl groups. This polysaccharide, which dissolves in cold water to produce high viscosity solutions, compares well with xanthan. It has a good pseudoplasticity, which is stable within a temperature range from 4 to 93 °C and a pH range from 3.0 to 12.0. It has also excellent stability and compatibility with high concentrations of salts such as 26 percent NaCl and 32 percent $CaCl_2$.

T. bombicola (ATCC 22214), a yeast, produces a biosurfactant, which is mostly glycolipids (Cooper and Raddock, 1984). The surfactant is produced in the late exponential phase. The substrates required are glucose or vegetable oil. The final yield of the surfactant reported is 70 g/L on the combination of substrates. At pH 4, the critical micelle concentration of the biosurfactant is 82 mg/L and the minimum surface tension is 37 mN/m. The surface tension is insensitive to concentrations of either NaCl or $CaCl_2$ up to 100 mg/L. The solubility of glylcolipids in water is pH dependent, with an optimum at pH 4. Therefore, T. bombicola is a promising organism for biosurfactant production.

4.2 Oil From Oil Shale and Tar Sands

Oil shale represents a major resource for the production of fuels and energy. Large deposits of oil shale in the Western United States, as well as other deposits in the Southeast, may be utilized to produce significant quantities of fuels or chemicals. Tar sands contain oil too viscous to produce by conventional recovery techniques and also represent a valuable raw material source. Thus, methods of efficiently and cheaply removing oil from shale and tar sands are of significant commercial interest.

A typical process for recovering fuels from oil shale consists of a retort with associated gas/solids separator and a quenching cooler for volatile products, a fluidized bed combustor (FBC) with associated cyclones, hoppers for the storage of solids, an air/flue gas heater exchanger, a waste heat boiler and a waste solids cooler. Many types of retorts may be used including a rotary bed, a fluidized or semi-fluidized bed, or a mechanical mixer. Typical oil yields are in the range of 70 liters per metric ton of shale.

The products from the retorting of kerogen (the organic fraction of oil shale) include shale oil, as the major product, as well as hydrocarbon gases (including hydrogen and CO), water, carbon dioxide, hydrogen sulfide, char and numerous minor components (Poulson et al., 1972). The hydrocarbon gases are composed of C_1-C_4 and C_5^+ hydrocarbon gases, with small amounts of H_2, CO, sulfur compounds and nitrogen compounds. An elemental analysis of the shale oil shows that it contains about 10 percent nitrogen, sulfur and oxygen compounds, in addition to carbon and hydrogen.

There are several major problems associated with the economical extraction of oil from shale. The kerogen is bound in a matrix of calcium and silica rock in a weight ratio of only about 1:15. Consequently, large quantities of refractary materials are necessarily mined and processed to separate the kerogen. The materials handling and energy requirements to process this inert material are substantial and represent a major portion of the capital and operating costs. Environmental problems include disposal of large quantities of spent shale and production of various gaseous and liquid pollutants. Separation of the shale from the limestone in situ, perhaps after mining but prior to retorting, would significantly enhance the efficiency and economics of shale oil processes and substantially reduce environmental problems.

Another pernicious economic factor is the presence of high concentrations of nitrogen, sulfur and oxygen compounds in the oil from shale. These components cause instability problems in the oil, poison catalysts in hydro-treating and fluid catalytic cracking and, of course, would create NO_x and SO_2 problems upon combustion. The traditional method of removing nitrogen, sulfur and oxygen compounds from oil is by hydrotreating. Hydrotreating increases the hydrogen content of the oil and decreases the content of hetero-atom (nitrogen, oxygen, sulfur) compounds (Frost et al., 1972; Montgomery, 1968; Sullivan et al., 1977). Temperatures of 300–400 °C are required for the treatment, with pressures as high as 1500 psi. This added treatment process requires a source of hydrogen, as well as energy, and detracts from the economic desirability of shale oil in comparison with crude oil.

A by-product of the retorting of oil shale is a gaseous hydrocarbon mixture consisting of C_1 and higher hydrocarbon gases, CO, H_2, CO_2, H_2S and H_2O. This gas is generally used as a fuel, but contains valuable feedstocks which could be converted to higher value chemicals. Increasing the fuel value and the production of chemicals from this gas stream could add substantially to the revenue from shale oil processes.

Raw shale contains significant amounts of limestone, dolomite and carbonates which can be readily attached by microorganisms. This matrix may be partially dissolved by acids produced by the biological activity of microorganisms:

$$CaCO_3 + H_2SO_4 \rightarrow CO_2 + CaSO_4 + H_2O \qquad (14)$$

$$CaO + H_2SO_4 \rightarrow CaSO_4 + H_2O \qquad (15)$$

Thus, bioleaching by microorganism attach on the shale oil matrix offers a promising technique for enhancing bioconversion of kerogen.

The application of in situ bioleaching to a full-scale oil shale recovery operation could eliminate much of the equipment and energy needed for mining, crushing, transportation and the disposal of waste material. Pretreatment of shale by bioleaching could convert most of the mineral matrix to a precipitate powder, easily removed by screening. The pretreated shale would be enriched in organic material, making recovery more efficient. Since substantial quantities of kerogen remain with the spent shale (up to 40 percent), bioleaching also offers an opportunity to measurably increase oil yields.

The biological removal of oil from tar sands may be accomplished by contacting the tar sands with organisms isolated from natural sources. The mechanism of attack is unknown but could be related to the formation of biosurfactants or the direct attack of organisms on the oil matrix. The technology closely follows the biological removal of oil from kerogen.

4.3 Economic Considerations

Busche (1982) estimated the costs of various tertiary oil recovery techniques and their potential impact on production. This information includes both biological and non-biological techniques and is summarized in table 117. Brashear and Kuuskraa (1978) noted that the impact of the various EOR technologies will depend significantly on decisions by Congress and the Administration, as well as public and private R & D activities.

Table 117. Costs of various tertiary oil recovery techniques (Busche, 1982)

EOR Technique	\$/bbl	Additional Production (percent)
Steam Drive	21-35	25-64
Fire Flood	25-37	28-39
CO_2 Drive	26-39	15-19
Polymer Flood	19-43	4
Surfactants/Polymer	35-47	30-43

5. Reactor Design and Operation

Reactor design, particularly for gas phase reactants, is an important consideration. Biological reactions are generally carried out in an aqueous environment where the microorganisms are suspended as single cells or in flocs. The reactants, present in the gas phase, must absorb across the gas liquid interface and diffuse through the culture medium to the cell surface to be consumed by the microorganisms. While absorption of oxygen from air into a fermentation broth is only one of many processes of gas absorption, probably no other aspect of the fermentation process has received so much attention from chemical engineers as the agitation and aeration of the culture medium (Finn, 1954; Calderbank and Blakebrough, 1967). The basic principles of oxygen transfer apply to the processes considered here. On the other hand, because air is used as the source of oxygen for aerobic fermentations, oxygen conversion or economy is not an important aspect of aeration studies. However, it is usually the depletion and conversion of the gaseous substrate that is the major consideration when gases other than air are involved, both in removal or production oriented processes. Operation under mass transfer-limited conditions helps to avoid possible inhibition by high dissolved concentrations of the gaseous substrates, and allows full utilization of the equipment capabilities and the energy required to create good phase contact. In the absence of any special bacterial requirements (such as adequate selection of biochemical pathways), it is most likely that industrial scale reactors will operate in mass transfer-limited regimes. The control of nutrient levels and dilution rates can be usually manipulated to allow the growth of microorganisms above concentration levels that ensure complete depletion of the dissolved gaseous substrate.

The transfer of gases in fermentation systems involves three phases: gas, culture medium and microbial cells suspended in the medium. In general, a combination of the following resistances can be expected (Bailey and Ollis, 1986):

1. Diffusion from the bulk gas to the gas-liquid interface;

2. Movement across the gas-liquid interface;
3. Diffusion of the solute through the relatively unmixed liquid region (film) adjacent to the bubble into the well-mixed liquid;
4. Transport of the solute through the bulk liquid to a second stagnant film surrounding the microbial species;
5. Transport through the second unmixed liquid region associated with the microbes;
6. Diffusive transport into the microbial floc, mycelia, or particle, if appropriate. (When the microbes take the form of individual cells, this resistance disappears); and,
7. Consumption of the solute by biochemical reaction within the microorganism.

The diffusion of products, of course, occurs in the reverse direction. As is the case with the conventional chemical engineering analysis of absorption processes, interfacial resistance in the gas phase to mass transfer through the bulk liquid is assumed to be negligible. Finally, when individual cells are suspended in a medium, the liquid film resistance around the cells is usually neglected with respect to other resistances, because of the minute size and the enormous total surface of the cells (Finn, 1954). Thus, for the transfer of sparingly soluble gases, such as CO, the primary resistance to transport lies in the liquid film at the gas-liquid film interface.

The choice of a suitable reactor for gas-liquid reaction or adsorption is very often a question of matching the reaction kinetics with the capabilities of the proposed reactor. In the case of biological systems, special care must be taken to insure the viability of the biocatalyst at the operating conditions. The specific interfacial area, liquid holdup and mass transfer coefficients are the most significant characteristics of a reactor, and special schemes have been devised to maximize mass transfer. Mechanically agitated reactors, bubble columns, packed columns, plate columns, spray columns, gas-lift reactors, etc. are examples of various kinds of contacting systems employed in these type of processes.

5.1 The CSTR

The traditional reactor used in fermentation processes is the continuous stirred tank reactor, or CSTR. As it relates to gas phase substrates, the CSTR has continuous gas flow into a constant volume liquid phase reactor. A small liquid feed stream is utilized to supply nutrients to the microorganism in the reactor system and to remove products. The agitation rate of the system is relatively high in order to promote transfer of the sparingly soluble gas into the liquid culture medium. A schematic of an experimental setup used in these studies is shown in figure 81.

Experiments have been conducted with P. productus for the production of acetic acid in a stirred tank reactor under two different operating regimes: one in which the overall performance is limited by the microbial biocatalytic reaction, and a second where the rate of transport of the gaseous substrate into solution controls the global process. In the first case, information about the intrinsic rates of growth and uptake by the microorganisms in continuous culture can be obtained for this growth mediated reaction. Operation under mass transfer limited conditions allows the development of suitable equations for modeling and process scale-up.

The easiest way to operate under non-mass transfer-limited conditions is to maintain a low cell concentration inside the reactor. Low cell concentration levels are achieved by using relatively high liquid dilution rates. The dilution rate is defined as the ratio of flow rate to the system to the reactor volume. Various steady states at different cell concentrations can be achieved in this manner. The overall rate data can then be used to determine specific microbial rates. While such an approach seems straightforward, two serious problems result in practice. First, due to the relatively low liquid dilution rates needed in avoiding washout when working with strict anaerobic bacteria, achievement of each steady-state conditions using conventional laboratory-scale fermenters requires a long operating time. Second, due to the inherent instability of the system, where small variations in agitation rate or in the foaming characteristics of the liquid lead to important changes in overall performance, data obtained over a wide time interval are sometimes in conflict. In this study, a non-steady-state procedure was employed to evaluate the microbial intrinsic rates in an interval of 5–6 hours. The procedure avoids the inconveniences of steady-state approaches and permits faster evaluation of the biocatalysts under various operating conditions.

The reactor was operated at steady-state at a high dilution rate and suddenly switched to a low dilution rate. The use of material balances written for the non-steady-state reactor operation in conjunction with the experimental data collected amount the period following the sudden change in dilution rate allows the evaluation of the rates of

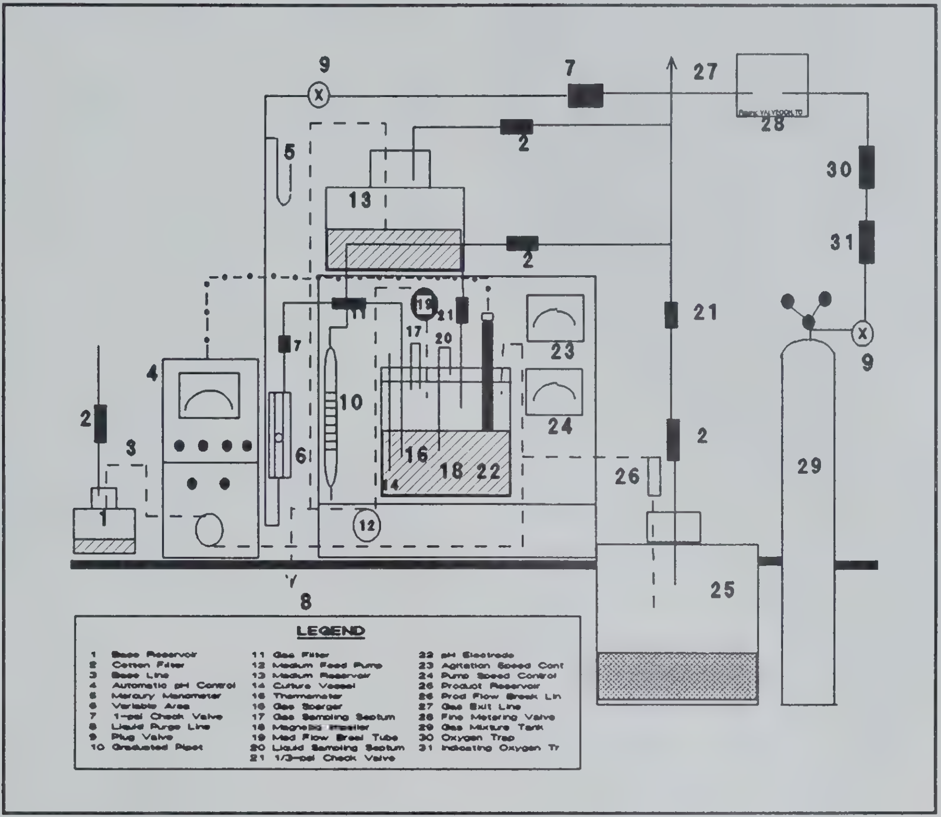

Fig. 81. Schematic of the CSTR system.

carbon monoxide uptake (${}^{r}{}_{\mathrm{CO}}$), growth (r_x), and production (r_p) during the experiment. Figure 82 presents these rates as a function of the cell concentration in the reactor. The slopes of these lines before they become independent of cell concentration (which corresponds to mass transfer limited operating regime) permit the determination of the specific rates of cell growth, carbon monoxide uptake and acetate formation. The parameters obtained agree with those obtained in batch culture when other fermentable carbon sources such as yeast extract are available to the bacteria (Vega et al., 1988a).

Experiments have been conducted with P. productus in a CSTR at different gas flow rates under mass transfer-limited conditions. In these experiments, the progress of the reaction is followed by use of an inert component, whose partial pressure does not change throughout the system. Assuming perfect mixing in both the gas and the liquid phases, the outlet ratio of CO to an inert (Y) can be related to the operating parameters according to eq (16):

$$\frac{1}{Y_o}=\frac{1}{Y_i}+\frac{V_L}{V_i}\ \frac{K_La}{H}\ \frac{P_I^o}{n_I} \qquad (16)$$

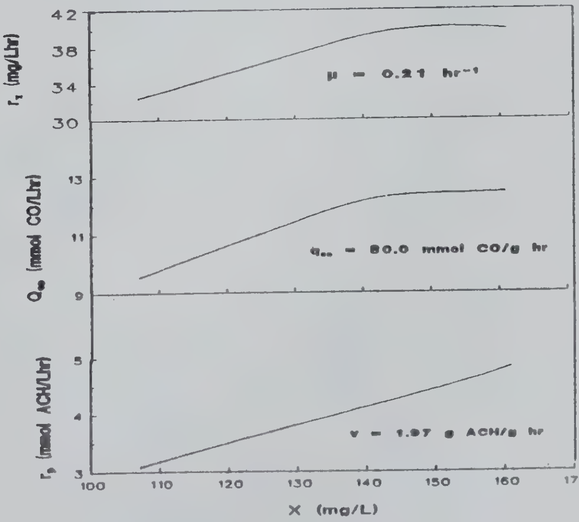

Fig. 82. Rates of growth, carbon monoxide uptake, and acetate production as a function of the cell concentration in the reactor.

where the subscripts o, i, I, and L refer to the outlet, inlet, inert and liquid. The term K_La represents the mass transfer coefficient, P represents partial pressure and V represents volume.

The agreement of the experimental data gathered with the model equation, as well as the procedure to evaluate the volumetric mass transfer coefficient achieved under the operating conditions, is shown in figure 83. A model including eq (16), as well as material balances for the gases flowing into the reactor and equilibrium relationships for the gas phase CO_2 with the bicarbonate and the pH level in the liquid, has been developed (Vega et al., 1988b). The solutions of the model for various volumetric mass transfer coefficients and various total operating pressures are shown in figures 84 and 85, respectively. Experimental data at 1 atm and a mass transfer coefficient of 30 are also included in the figures. As observed in the model results, increases in the mass transfer coefficient or in total operating pressures lead to higher reactor productivities. Due to the perfect mixing in a CSTR, complete conversion is only possible when the gas flow rate is zero. Figure 84 shows that with a mass transfer coefficient of 100, a gas retention time (inverse flow rate per unit volume) of one hour (G/V_L-1) would result in a conversion of 80 percent. From figure 85, the retention time could be reduced to 6 minutes at 10 atm for the same amount of CO converted. The use of the model allows the extrapolation of performance of the CSTR system and will permit preliminary economic evaluation of an industrial scale process when coupled with suitable equations for scale-up of parameters such as the mass transfer coefficient.

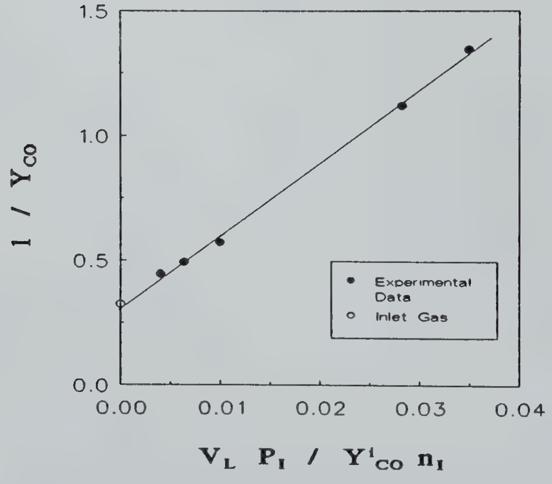

Fig. 83. Model verification and evaluation of the volumetric mass transfer coefficient in a CSTR.

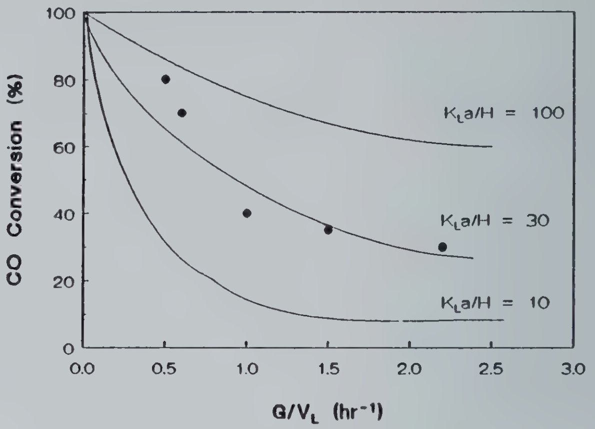

Fig. 84. Model results for carbon monoxide conversion as a function of the gas flow rate per unit of culture volume for various volumetric mass transfer coefficients (KLa/H in mmol CO/atm L hr).

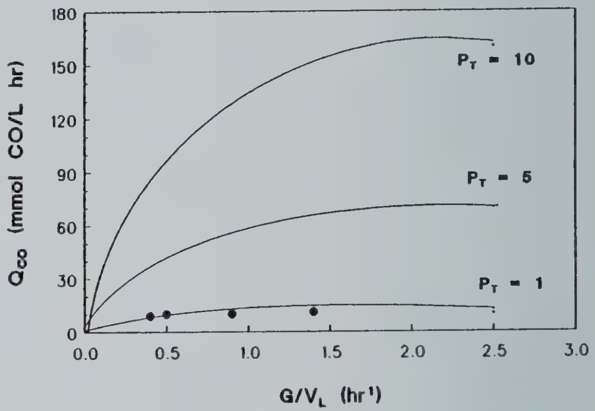

Fig. 85. Model results for carbon monoxide uptake as a function of the gas flow rate per unit of culture volume for various total operating pressures in a CSTR (PT in atm).

Mechanically agitated bubble contractors are very effective with viscous liquids or slurries and very low gas flow rates and large liquid volumes. They are also noted for the ease with which the intensity of agitation can be varied and heat can be removed. Their principal disadvantages are the cost of high agitation rates and the fact that the liquid and the gas phase are almost completely back-mixed which decreases the driving force for transport of the gas into the liquid and, as seen in figure 85, does not allow complete conversion of the inlet gas except at a zero gas flow rate.

5.2 Packed Bubble Column

Bubble columns are commonly used in industrial processes, both as reactors or absorbers, whenever a large liquid retention time and/or a large liquid hold-up is needed. Some advantages of bubble columns are the elimination of mechanical agitation, minimum maintenance, relatively low costs, high interfacial area and high mass transfer coefficients (Charpentier, 1981). The principal disadvantages are a large extent of backmixing and coalescence. These two drawbacks can be minimized by employing packing inside the column.

Experiments have been conducted with P. productus in a packed bubble column at various gas flow rates in a manner similar to that in the CSTR studies. A schematic of the experimental setup used in these studies is shown in figure 86. For this system, assuming perfect plug flow in the gas phase ascending through the column and constant partial pressure of the inert gas in the system (as closely substantiated from experimental data), the outlet ratio of CO to the inert can be related to the operating conditions according to (Antorrena, 1987):

$$\ln \frac{Y_i}{Y_o} = \frac{K_La}{H} \quad \epsilon_L \quad \frac{ShRT}{G} \qquad (17)$$

In this equation, H represents the Henry's law constant, ϵ_L represents the porosity, S is the cross-sectional area, h is the height of the column, R is the ideal gas constant and T is the absolute temperature. A plot of ln Y_i/Y_o vs ShRT/G yields a straight line with slope $K_La\epsilon_L/H$ (fig. 87). Regression of the experimental data of this plot gives an operating value for $K_La\epsilon_L/H$ of about 13.5 mmol Co/atm·L·hr. The numerical solution (Runge-Kutta) of the differential equations that describe the system were then applied to other operating conditions of contacting are shown in figure 88. Experimental data are given for $K_La\epsilon_L/H$ of 13.5. The slight deviation of the experimental data with respect to the model predictions in figure 88 is due to departure from the assumptions in the derivation of eq (17). Comparison of figure 88 with that obtained for the CSTR (fig. 83) indicate the benefit of plug flow operation in the gas phase by allowing almost complete conversions at gas flow rates above zero.

The packed bubble column achieves higher rates of specific CO conversion than the stirred tank reactor without the need for more expensive mechanical agitation. More importantly, at the same mass

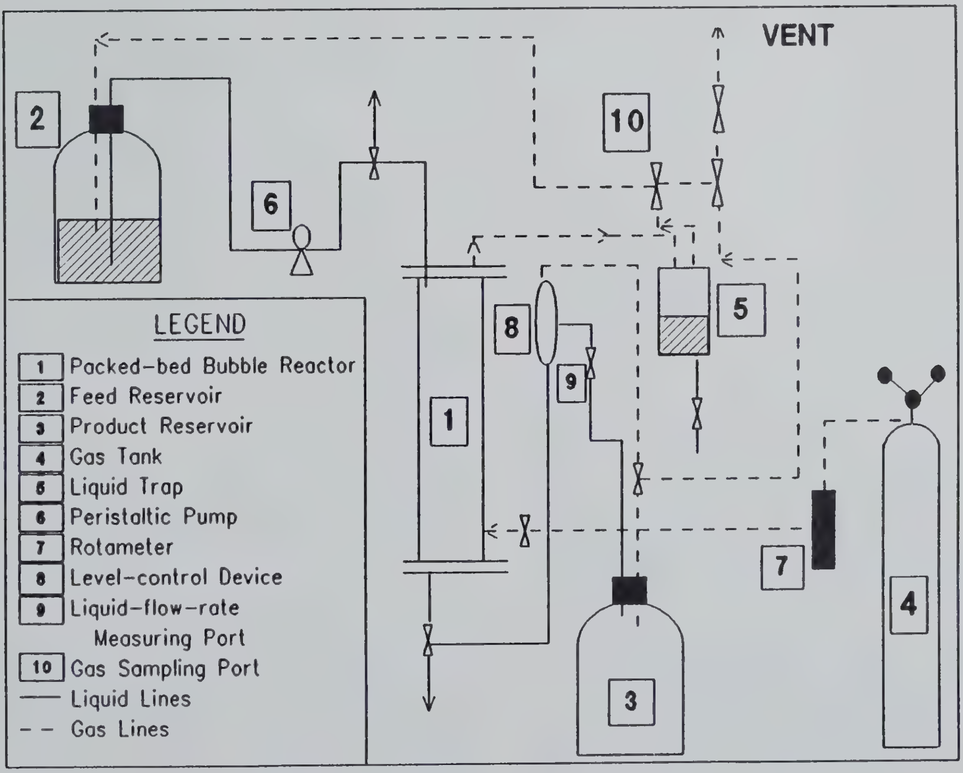

Fig. 86. Schematic of the packed-bubble reactor system.

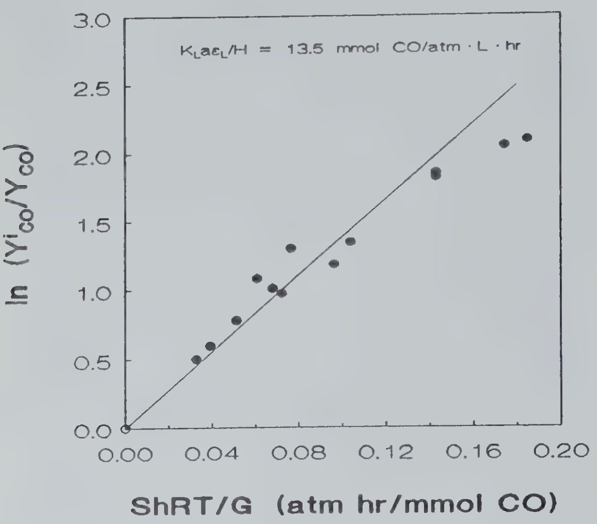

Fig. 87. Model verification and evaluation of the volumetric mass transfer coefficient in the packed bubble column.

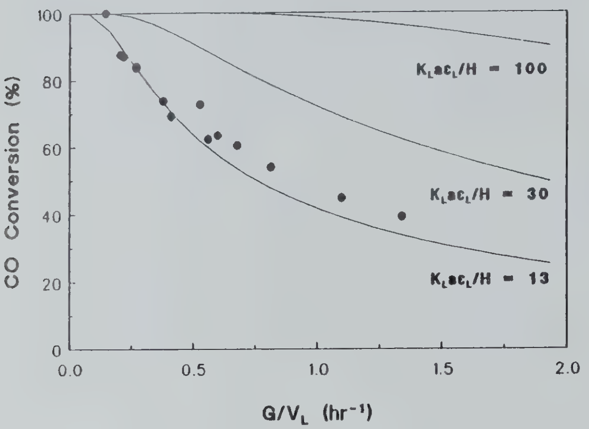

Fig. 88. Model results for the carbon monoxide conversion as a function of the gas flow rate per unit of culture volume for various volumetric mass transfer coefficients in a packed-bubble column (KLaEL/H in mmol CO/atm L hr).

transfer coefficients as in the CSTR, conversions are substantially higher. For example, at K_La/ H – 100, the conversion at a one hour retention time is 95 percent, compared to 80 percent for the CSTR. Alternatively, 50 percent conversion could be achieved in a retention time of 30 min in the bubble column with a K_La/H of only 30. The major disadvantage of a bubble or packed bubble column is the lack of flexibility in operating conditions since the contacting capabilities are mainly fixed with the design of the column dimensions and packing.

5.3 Packed Columns

Packed columns are used conventionally to obtain a low pressure drop or low liquid holdup when there is practically no heat to remove or supply, or the liquid is corrosive. They are usually operated countercurrently since a higher driving force can be achieved than with cocurrent operation. However, when an irreversible reaction occurs between the dissolved gases and the absorbent (as in biological systems), the mean concentration driving force is the same for both modes of operation. In this case, the capacity of cocurrent columns is not limited by flooding and at any given flow rates of gas and liquid the pressure drop in a cocurrent column is less (Charpentier, 1981).

Experiments have been conducted with P. productus in a cocurrent column packed with ceramic intalox saddles. A schematic of the system is shown in figure 89. In this experimental setup, the liquid and the gas are disengaged in a liquid/gas separator with the culture being recirculated back to the top of the column. In this manner, a high concentration of cells can be maintained inside the reactor while at the same time using high L/G operating conditions inside the column. For the results obtained in this column, the same general considerations used in the bubble column can be used and a model based on eq (17) can be developed.

The arrangement of the experimental data gathered with P. productus in the packed column at three different recirculation rates according to eq (17) is shown in figure 90. The slope of the lines obtained by linear regression of the data corresponds to the value of the volumetric mass transfer coefficient ($K_La\epsilon_L/H$) achieved at each operating condition. The experimental data for carbon monoxide conversion in the packed column at three liquid recirculation rates along with the model simulation are then presented in figure 91 as a function of the gas flow rates employs per unit of initial void volume in the column. The initial void volume has been chosen as the volume basis to allow direct comparison with the bubble column results, where the culture volume is the initial void volume. As observed in figure 91, the mass transfer capability of the column is greatly enhanced by increasing the liquid recirculation rate. At the highest recirculation rate employed, a $K_La\epsilon_L/H$ value around 30 mmol CO/atm·L·hr was obtained, more than twice the value obtained during bubble column operation in the same reactor.

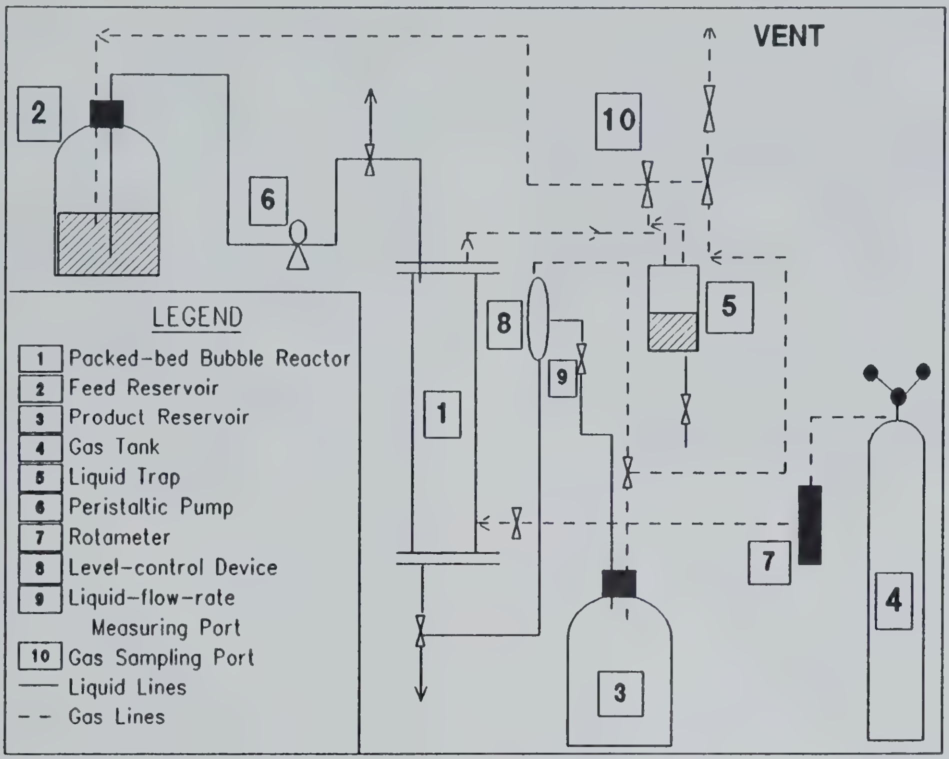

Fig. 89. Schematic of an absorption tower system with biocatalyst recirculation.

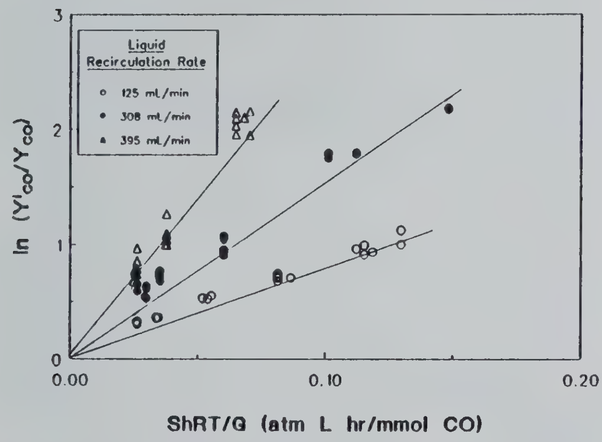

Fig. 90. Model verification and evaluation of the volumetric mass transfer coefficient in the packed column.

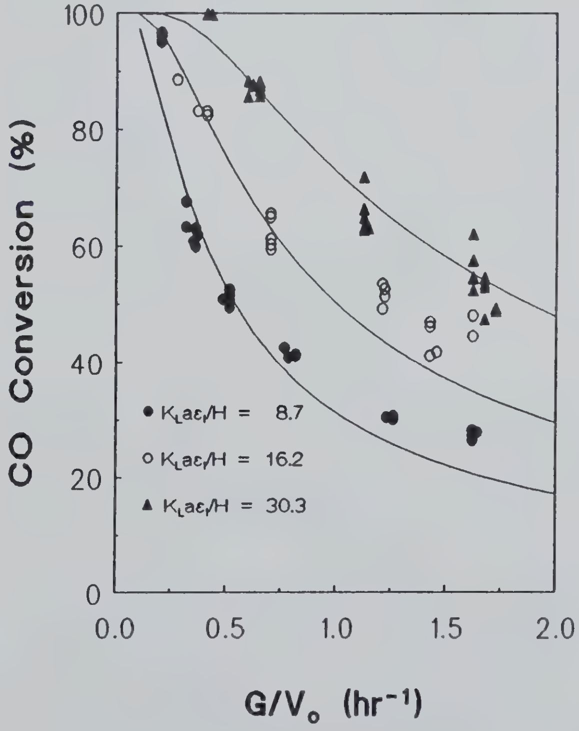

Fig. 91. Model results for carbon monoxide as a function of the gas flow rate per unit of initial column void volume for various volumetric mass transfer coefficients in a cocurrent packed column.

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Mineral Bioprocessing: Opportunities in Extractive Metallurgy and Environmental Control

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This chapter identifies biotechnical opportunities for metals' extraction and environmental control in mining. Considered are scientific and engineering needs, market size, competitive factors, patents and proprietary positions, and market/business strategies. Market opportunities for biotechnology in gold mining include (a) preventing adsorption of gold-cyanide complexes to carbon in the ore, (b) applying thermophilic bacteria to gold extraction, (c) identifying or genetically modifying organisms to produce gold complexing agents, and (d) designing reactors to augment bioextraction of gold. An estimated $100 million per year global opportunity exists for mitigation of environmental problems associated with mining. Opportunities are (a) biodegradation of cyanide species in aqueous and solid wastes, (b) biotreatment of acid mine drainage and other metal-bearing effluents, (c) biostabilization of sulfidic solid wastes and iron-arsenic precipitates, (d) bioflocculation of mineral fines and (e) biodegradation of organic, mineral-processing reagents. The industrial mineral, fossil fuel and base metal sectors also offer potential market opportunities in preventing biodeterioration of concrete and stone constructions, desulfurizing coal and petroleum, and bioleaching of base metal minerals, respectively. Important market considerations include (a) defining products and services, (b) pricing, (c) tailoring processes to specific ores and environments, (d) demonstrating viability and robustness of microorganisms/enzymes, (e) validating economics in long-term tests, (f) merging biotechnical and physical/chemical processes, (g) overcoming communication barriers between industries, and (h) developing workable market strategies.

Key words: biodegradation; biohydrometallurgy; bioleaching; environment; gold extraction; metals; minerals; solid mine waste; water treatment.

1. Introduction

Mining in the United States today is a rapidly modernizing industry with on-going introduction of high technology products and processes. Biotechnology promises to play an increasingly significant role in maintaining the mining industry's global competitiveness. Problems facing the industry are high energy costs, lower-grade and harder-to-process (refractory) mineral reserves[1] and resources,[2] and increasingly restrictive environmental regulations. Technical fine-tuning of processes, rigorous pilot-plant tests and creative business strategies are necessary for biotechnology to achieve commercial reality in the mining industry.

This chapter (a) summarizes the needs of the mining industry, (b) translates these needs into biotechnical opportunities, (c) summarizes technological deficiencies and obstacles impeding transfer of biotechnology into the industry, and (d) recommends strategies to overcome barriers.

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[1] Reserves are known, identified deposits from which a mineral product can be extracted profitably with existing technology under present economic conditions.

[2] Resources include reserves and deposits not economically or technologically recoverable at present.

Introducing biotechnology to the mining industry is different from marketing biotechnology to the health care, chemical and agricultural business sectors. The inability of the mining and biotechnology industries to communicate on the same plane is the principal reason. The biotechnology industry usually doesn't have a clear understanding of the needs and constraints of the mining industry. Likewise, the mining industry doesn't have a definitive understanding of what biotechnology has to offer or even how biotechnology relates to mining.

Section 2 sets forth a brief historical perspective of the mining industry and reviews fundamental changes shaping the industry's future in the United States and abroad. The remainder of this chapter identifies how these changes translate to industrial needs and how biotechnical developments can meet these needs.

2. Mining: A Changing Industry In A Changing World

2.1 Historical View

Mining has always been viewed as a dirty, dangerous, noisy, environmentally destructive [1] and highly cyclical business. From the early days of mining through the middle of this century this image has largely been true. From 1950 through 1975 significant technological changes (for example, the introduction of bacterial leaching of low-grade copper ores), increased environmental regulations, and substantial improvements in health and safety took place in the mining industry. By the late 1970's the U.S. mining industry was booming, with the copper industry alone contributing more than $6 billion to the gross national product and employing well over 90,000 people [2].

Although great strides were made in many aspects of mining, the cyclical business aspect remained. In the early 1980's the U.S. mining industry was faced with (a) high energy costs, (b) low ore grades, (c) increased trade union demands, (d) competitive foreign imports, (e) outdated equipment and in some cases outmoded technology, (f) increased environmental demands, and (g) a collapsed nuclear power industry. These events contributed to mine closures, reduced production capacity, substantial lay-offs and even the complete disappearance of large companies (for example, Anaconda Company). By the late 1980's the mining industry had phased-out high cost operations, modernized facilities, automated, converted to technologically and environmentally superior processes, restructured businesses, and reduced labor and wage rates [2]. Today the U.S. mining industry is small and globally competitive for most mineral commodities. Environmental compliance is now a management priority. The industry is also gradually cleaning up the environmental legacy of past mining activities.

2.2 Mining in the 21st Century

The mining industry has made great forward strides in over-coming problems with mineral processing, environmental compliance and foreign competition. However, much more must be accomplished for the industry to remain in business in the 1990's and beyond. In addition to technological advancement, the industry must effectively deal with the intense public scrutiny it now faces.

In the last decade important biotechnology advances applicable to mineral processing and the mining environment have been made. These advances are expected to play an important role in (a) providing innovative and cost effective processes to solve some of the industry's needs, and (b) improving the industry's public image by problem-solving through high-technology approaches. Segments of the mining industry that could potentially benefit from biotechnology are the environment, precious and base metal mining, fossil fuel processing, and industrial mineral mining and corrosion prevention.

3. Biotechnology and Mining: Market Opportunities and Entrepreneurial Approaches

This following section discusses:

- Technological problems facing the mining industry;
- Biotechnical developments applicable to these problems;
- Scientific and engineering needs for commercially viable biotechnical processes;
- Competitive factors that may be barriers to market entry of biotechnology;
- Patent and proprietary positions, regulatory aspects and raw material requirements, if applicable; and
- Estimated market potential

3.1 Environmental Control in Mining and Mineral Processing

Mining is not environmentally benign. The industry is concerned not only with substantive present and future environmental matters, but is faced with massive clean-up of mine wastes generated decades ago. Table 118 tabulates environmental problems and issues by mine sector and relates possible biotechnical solutions to these environmental problems. Necessary biotechnical developments are noted, competitive processes are listed and relevant biotechnology discoveries and patents are referenced.

Probably the greatest barrier to the introduction of biotechnology for waste treatment in the mining industry is the reluctance by the industry to employ unconventional technologies that do not have a history of use. If conventional technologies, such as lime or sulfide precipitation and ferric iron coagulation, solve the problem, these processes will be employed even if biotechnical processes are offered at lower cost. However, with increasingly restrictive discharge standards (for example, biomonitoring standards) becoming more prevalent, conventional technologies sometimes can't achieve the restrictive limitations. Also, situations exist (for example, cyanide degradation in solid mine wastes) where no technology is available. Under these circumstances novel processes are usually evaluated by the mining industry, and, if demonstrated to be technologically viable and cost effective, are embraced. The business approach, therefore, should be to perform a thorough market analysis of the mining industry. Those environmental problems, for which there is a sizeable market and for which existing technology is inadequate or non-existent, should be targeted for bioprocess development. From those problems listed on table 118 the most significant market opportunities with the least competition are (a) closure of spent, heap-leach[3] operations 5–10 years before full market potential, (b) stabilization of acid-generating, solid mine wastes (immediate opportunity), and (c) treatment of large flows of aqueous wastes with dilute concentrations of mixed metals (rapidly developing opportunity with full potential developing in 5–10 years). Over the next 10–20 years these collective opportunities on a global basis are estimated to exceed $100 million annually.

Most of the processes discussed in table 118 employ viable microorganisms. The recommended strategy for these opportunities is to market turnkey systems in which the microorganisms are integrated into a fully engineered unit. Therefore, products would include hardware and proprietary technology coupled with on-going services. In the case of biosorbents, the product would probably be marketed more like a reagent or ion-exchange resin.

Entrepreneurs building a business selling biosorbents are advised that raw material supplies should be a prime consideration. If genetically altered microorganisms are the basis of the product, significant advances must be made in product performance to compensate for the additional cost of growing the organisms. If waste microorganisms (for example, fungal or bacterial biomass from the pharmaceutical industry) are to be used, caution must be taken in securing a long-term supply that is consistent in quality and is uncontaminated. When using waste microorganisms, genetically engineered for pharmaceutical or enzyme manufacturing, other issues must be addressed. The company generating the waste biomass may be concerned about its genetically altered microorganism falling into the hands of competitors. Also, the potential of releasing genetically altered organisms into the environment must be considered, even though the alteration was for product production not environmental clean-up.

3.2 Gold Mining

3.2.1 The Refractory Ore Problem. For the most part the gold industry mines oxide gold ores. These ores, which have been abundant, respond well to the cyanidation method of extraction. The cyanidation process entails crushing the ore and mixing the crushed ore with cyanide in a ball mill. The gold forms a soluble complex with the cyanide. The gold-cyanide complex is removed from the mixture by adsorbing the complex onto activated carbon. Oxide gold ores that are low-grade are crushed, re-agglomerated with cement, piled onto lined pads and leached with a dilute cyanide solution that is dripped or sprinkled over the ore. This process is called heap leaching. The relative terms, low-grade and high-grade ores, are used without assigning concentration values. These values change based on mining and extraction costs, the price of gold and other considerations. Throughout the world, reserves of oxide gold ores are being depleted and most long-term gold resources are

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[3] Heap leaching of gold entails stacking crushed ore on pads and applying cyanide. After the gold is extracted, the heaps are rinsed with water to remove residual cyanide and soluble metals.

Table 118. Environmental problems in the mining industry and possible biotechnical solutions

Environmental problem	Sectors affected	Biotechnology solution	References	Issues	Needed biotechnical developments	Competitive processes
Cyanide-containing, aqueous discharges	Gold & base metal mining	Cyanide-degrading microorganisms	[3, 4, 5, 6, 7]	Refractory metal-cyanide complexes are not degraded; concern exists about long-term stability of iron-cyanide complexes; there is a requirement for rapid kinetics	Microbes that degrade weak-acid-dissociable, metal-cyanide complexes	Chemical oxidation (e.g., chlorination, hydrogen peroxide); Fe(II) addition
Closure of spent, cyanide, heap-leach operations	Gold mining	In-situ degradation of cyanide in spend heap-leach residues	[8, 9]	Cyanide is ineffectively washed from spent ores to mandated levels; variable conditions in heaps exacerbate clean-up	Microbes able to degrade cyanide in presence of spent ore and function under variable physical, chemical and mineralogical conditions	Exhaustive water washing followed by chemical oxidation of wash-water
Acid mine drainages	Base and precious metal mining; inactive & abandoned mines; coal mining	Wetlands; biosorption products; microbial sulfate-reduction	[10, 11, 12, 13, 14]	Acid neutralization is often required before biotechnology treatment; some metals are not effectively removed; there is insufficient metal loading on biosorbents; potential regulatory problems exist with wetlands (e.g. metal volatilization & metal loading in sediments)	Better control of wetland biotechnology; microbial sulfate-reduction in controlled reactors; biosorbents that remove oxy-anions (Se, As), selectively remove metals & possess greater loading capacity	Lime precipitation; sulfide precipitation
Final disposition of solid mine wastes with acid-generating capability	Base and precious metal mining; inactive & abandoned mines; coal mining; uranium mining	Stabilization of solid mine wastes using ecological engineering measures; inhibit microbial sulfur & iron oxidation using biocides or eliminate oxygen & water	[15, 16, 17, 18, 19]	There has been inadequate long-term testing of biotech processes; better control of biotech mitigation measures must be implemented; there is a need for continued application of biocides for thiobacilli; acid generation & soluble metal production continues after inactivating thiobacilli	Development of controllable biotechnology method for reversing metal solubilization (e.g. biological sulfate reduction); biotechnical process to "plug" acid-generating solids mine wastes (e.g. microbial polymers to prevent air and water entry)	Surfactant products to inhibit thiobacilli; compacted clay layers; revegetation
Treatment of large flow-volumes of groundwater, tunnel discharges, & mine dewatering products containing low concentrations of mixed metal cations, anions & radionuclides	Base and precious metal mining; inactive & abandoned mines; coal mining; uranium mining	Microbial-based products capable of effectively removing metals with low initial concentrations to achieve less than detectable levels	[10, 11, 20, 21]	Technology needs to be (a) scaled to treat large flows (500 million liters/day), (b) effective with minimal retention times, (c) applicable using conventional & compact treatment plants, and (d) achievable at low cost	Genetically optimized living organisms in contained systems; development of designer biochemicals with high affinity metal-binding sites employable in counter-current systems to minimize product volume	Chemical precipitants; ion exchange
Disposal of soluble iron-arsenic wastes generated from hydrometallurgical processing of sulfidic-refractory gold ores	Gold mining	Microbial-based technology to produce iron arsenate compounds with long-term environmental stability	[10, 11, 20, 21]	The long-term stability of iron-arsenate precipitates is debatable. With increased hydrometallurgical processing of refractory gold ores greater quantities of soluble Fe & As will require treatment & disposal	Confirmation that biotechnology plays a role in producing environmentally stable wastes and development of applicable technology	Lime and/or iron addition
Settling of suspended particulates (mineral fines) in process waters	Coal, phosphate and iron ore mining	Employ microorganisms or microbial polymers for aggregating clays and mineral fines	[24, 25, 26, 27]	Mineral values are lost and reclamation delayed through the inability to flocculate fine mineral particles. Synthetic polymers are largely ineffective	Exhaustively evaluate existing microbial polymers and/or develop through genetic manipulation ideal, cost-effective, biotechnical solution	Synthetic polymers
Degradation of organic, mineral processing reagents (flotation reagents, flocculants, dispersants, solvent extraction reagents, etc.)	Base and precious metal mining; phosphate mining; coal mining	Adapt bioremediation of refractory organic compounds to degradation of organic mineral processing chemicals	[14, 28, 29]	A wide variety of organic reagents are employed in mineral processing. The transport and fate of these chemicals is not well studied. Effluents containing these reagents are discharged and regulated	Basic studies on degradation of standard collectors, frothers, flocculants and dispersants are needed with commensurate development of bio-treatment processes	Chemical oxidation; natural attenuation with clays and mineral particles

sulfidic in nature. These ores are termed "sulfidic-refractory." They are characterized by sub-micron sized, elemental gold physically embedded in a sulfide mineral matrix, which is pyrite (FeS2), arsenopyrite (FeAsS), or both. When treated with cyanide, these ores often yield less than 20% of the gold. Poor gold recoveries occur because the cyanide is unable to penetrate the sulfide mineral matrix and react with the embedded gold [30]. Extremely fine grinding enhances gold extraction by cyanide, but fine grinding is not cost effective due to energy losses associated with comminution. Alternative technologies for treatment of high-grade, sulfidic-refractory gold ores are:

(a) Roasting, whereby a high-grade ore or concentrate[4] is treated at high temperature to oxidize the sulfide to SO_2 [31], and

(b) Pressure oxidation, whereby the gold ore or concentrate is treated under high oxygen pressure to oxidize the sulfides to sulfuric acid [32].

Roasting is capital intensive and state-of-the-art air scrubbers must be installed to capture SO_2 and volatile metals. Pressure oxidation is also capital intensive. Additionally, pressure oxidation can be hard to manage from an operator's standpoint as high sulfide content results in intense heating and possible explosive reactions. During the process all of the sulfide is converted to sulfuric acid resulting in a waste treatment problem. Neither roasting nor pressure oxidation is suitable for treating low-grade, sulfidic-refractory gold ores because of high capital and operating costs.

Some gold ores are also refractory due to the presence of carbonaceous material similar to graphite. These ores are designated "carbon-aceous-sulfidic-refractory." The contaminant carbon tends to re-adsorb the soluble gold-cyanide complex in a adsorptive reaction competitive to that of activated carbon [30]. No technology other than roasting has yet been developed to satisfactorily mitigate the competitive adsorption. The industry is currently stockpiling low-grade ores until technology is developed.

3.2.2 State-of-the-Art of Biotechnical Applications. Bioleaching of sulfidic-refractory gold ores is a process development of the last decade, although the fundamentals of bioleaching sulfide minerals have been studied since the late 1950's [33,34]. *Thiobacillus ferrooxidans*, *T. thiooxidans* and *Leptospirillum ferrooxidans*, which are aerobic, extremely acidophilic bacteria that derive energy from the oxidation of iron and/or sulfur compounds, degrade the pyrite and arsenopyrite matrices exposing the elemental gold. For many sulfidic-refractory gold ores about 50% of the pyrite or arsenopyrite needs to be oxidized to expose greater than 90% of the gold [35]. However, for some sulfidic-refractory gold ores 90% of the sulfidic material must be oxidized to recovery 90% of the gold. Not all of these latter ores are candidates for bioleaching, because of the lengthy time required for sulfide oxidation. After sufficient bioleaching of the gold ore (this is called "pretreatment") has taken place, the gold ores are (a) water washed to remove acid, soluble ferric iron and other soluble metals, such as copper, zinc, etc., (b) neutralized with lime, and (c) treated with a cyanide solution to solubilize the exposed gold. In the laboratory gold recoveries can exceed 95% unless the ores are also carbonaceous-sulfidic-refractory.

Bioleaching of sulfidic-refractory gold concentrates, that is, gold ores containing sulfide minerals concentrated by gravity or flotation, is practiced commercially in stirred-tank reactors in South Africa [36], Australia and South America. This process entails agitation of the concentrate in an acid solution injected with air. Now under development bio-heap leaching of gold ores [37] involves placing crushed ore onto impermeable pads and using bacteria to solubilize mineral sulfides. Once the sulfides are sufficiently oxidized the ore must be thoroughly washed to remove acid and soluble metals before cyanide is used to solubilize the gold.

Patents covering the application of bioleaching in pretreatment of refractory gold ores have issued [39,40]. Companies using bioleaching in tanks and heaps also guard their technology with trade-secrets and confidential know-how.

3.2.3 Biotechnical Opportunities. Opportunities in gold extraction include (a) mitigating adsorption of gold-cyanide complexes to carbon in the ore, (b) using thermophilic bacteria, (c) applying microorganisms that produce cyanide or other substances that solubilize gold, and (d) improving engineering designs for leach tanks and heaps.

Although global resources of carbonaceous-sulfidic-refractory gold ores can not be accurately quantified at this time, these resources are estimated as substantial. At present roasting is the only treatment alternative for these refractory ores. Because of the cost of roasting, ore grades must be high to employ this technology. A cost-effective microbial or enzymatic process to render the carbonaceous matter inactive, i.e., prevent the gold-cyanide complex from adsorbing onto the contaminant carbon [30], would allow processing of lower-grade ores and likely result in substantial cost savings over roasting. Complete biodegradation of the carbonaceous component is probably unrealistic because of the refractory nature of the carbon and the real possibility of creating a massive waste treatment problem. Alteration of the carbon by direct microbial action or by microbial products produced in-situ or ex-situ appears to be viable. Two patents [37,38] describe carbon deactivation with a microbial consortium, however, further efforts are necessary on this front.

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[4] Concentrates are obtained by up-grading the ore-bearing mineral with gravity separation or flotation technology to separate the ore from useless rock.

Bioleaching of sulfide minerals is an exothermic process. When gold concentrates or gold ore with sufficiently high amounts of sulfide mineralization are subjected to bioleaching in stirred-tank reactors, heat must be dissipated to prevent overheating and inactivation of *Thiobacillus* and *Leptospirillum* species [41]. Employing thermophilic, chemolithotrophic bacteria is under consideration [30,42,43]. Drawbacks with use of some thermophiles are their inability to adapt to high pulp densities of ore (i.e., the ratio of solids to liquid) [44] and the possible lack of robust qualities needed for commercial applications. These drawbacks must be overcome before thermophilic bioleaching of refractory gold ores is economic. Additionally, large-scale testing over an ample time period is required to demonstrate feasibility of the thermophiles in stirred-tank reactors and more study is necessary to determine what role, if any, these organisms would play in bio-heap leach operations.

Cyanide is conventionally used to solubilize gold. However, alternative reagents are desirable because of (a) the environmental sensitivity of cyanide, (b) the need to find a gold complexing reagent that doesn't adsorb to contaminant carbon in the ore, and (c) the desirability of finding a reagent that can be used to solubilize gold under acid conditions [45]. The latter need is very important in bacterial pretreatment of gold ores as pretreatment is accomplished under very acidic conditions. Microorganisms producing substances that solubilize gold in-situ may be one alternative. Cyanide production by microorganisms is known and the process patented for gold leaching application [46]. The potential to discover other naturally occurring organisms that have gold-solubilizing capability or to genetically create such a microbe is good.

Bacterial sulfide degradation is an aerobic process and getting oxygen in sufficient quantities to the microorganisms in a stirred-tank reactor or bio-heap leach operation is a problem. Better engineered reactors and novel constructions of bio-heap leach piles to improve oxygen transport to the microorganisms are needed.

3.2.4 Barriers and Approaches to Marketing Biotechnology to the Gold Industry. There are six principal obstacles affecting the introduction of biotechnology for gold extraction:

- Insufficient economic correlation between the process cost and the mineral value of the ore or concentrate;
- The marketing of "generic" technology when ore specificity plays a critical role;
- Inapplicable and/or insufficient large-scale tests to demonstrate long-term, technical viability;
- Naivety about the magnitude of the full-scale application;
- Lack of in-depth experience and knowledge about the interrelations among simultaneously occurring physical/chemical processes and biotechnical applications; and
- Issues concerning product/service definition and marketing strategies.

The ore grade of most large deposits today is really quite lean with most companies mining reserves of around 1.7 grams/metric ton (0.05 ounce/ton). At a gold price of say $350/oz a ton of rock is worth about $17.50, if 100% of the gold is recovered. Considering all of the costs that go into mining, processing, and other matters relating to the business, any biotechnical process must be very inexpensive to implement (e.g., less than $1/ton) or must have a significant impact on gold recovery. The market potential can be derived by estimation of the tonnages of refractory ores to be processed annually on a world-wide basis. This is a rapidly developing market in the United States, Canada, South Africa, Australia and possibly the Commonwealth of Independent States.

Ores from different deposits can exhibit vastly different behavior to extractive processes. For example, trace metals, such as mercury, may be toxic to the microorganisms or the sulfides may not respond well to bacterial leaching. These factors often necessitate tailoring biotechnical processes to specific ores. Not only does this negate marketing a technology as an off-the-shelf process to any company anywhere in the world, but requires scale-up and long-term testing of the process with a specific ore.

Large-scale and long-term testing is best done in concert with mine operations. This (1) provides a relatively steady supply of the general type of ore to be processed, (b) offers realistic adversities that can be encountered (e.g., freezing conditions, changes in feed grade, contamination with wild-type microorganisms, down-time, etc.), (c) gives insights into how biotechnical processes must be integrated with other physical/chemical processes, and (d) instills a sense of scale for full-fledged operations. Agreements with mine operators to accomplish large-scale testing can be difficult to establish, because the objectives of the mine operator and the biotechnology company are considerably different. Problem issues are (a) the high cost of field trials usually borne by the mine operator resulting in the mine operator controlling a percentage of the technology and/or possessing certain licensing rights that may affect other sales, (b) the real possibility of disinterest by the mine operator to market biotechnology to competitors, and (c) reluctance on the mine operator's part to release confidential data or to allow competitors on-site for marketing and sales purposes. The best way to overcome these potential difficulties is for the biotechnology company to be aware they exist and be prepared in negotiations to compensate for these difficulties.

3.3 Recovery of Silver From Manganiferous-Silver Ores

When silver is associated with manganese, the use of cyanide to extract the silver is impractical. Cyanide consumption is excessive and manganese can occlude the silver inhibiting the complexation reaction between the silver and the cyanide [47,48]. Silver can be recovered biologically using two different approaches: (a) leaching of the manganese, silver or both using metabolic products that complex the metals [47], and (b) reducing Mn(IV) microbially to Mn(II) liberating silver [48]. Both of these processes have been demonstrated at bench-scale. However, substantial biotechnical and engineering development remain before either of these technologies can be considered for commercial application.

At present manganiferous-silver ores are not mined, because of depressed silver prices and the dearth of viable processing options for this type of ore. Although manganese is a strategic metal, there was no domestic mine production of manganese in 1990 or 1991; manganese for production of steel and other minor uses is imported [49]. The need to process manganiferous silver ores would increase if the price of silver increased dramatically, manganese demand out-distanced supply, or foreign supplies became endangered. There is an estimated 36 million troy ounces of silver resources in the form of manganiferous-silver deposits in the United States [50]. Many of these deposits have high-grade silver and are rich in manganese. At present there appears to be a limited market opportunity for biotechnology to process refractory manganiferous-silver ores because of lack of demand for either the silver or the manganese.

3.4 Base Metal Mining and Processing

The single largest application of biotechnology in the mining industry is the bioleaching of low-grade, sulfidic copper ores in a process called "copper dump leaching." Although applied unwittingly for centuries by miners, the bioleaching process was researched, defined and purposefully applied in the 1950's. The process is now used throughout the western United States to extract copper from ores that would otherwise be uneconomical to process due to the low copper content [33,34]. Today this bioleaching process is applied throughout the world with the majority of the research, development and new applications now carried out in Chile.

Bioleaching of copper ores employs bacteria of the genus *Thiobacillus* to oxidize reduced iron and sulfur species releasing the copper into a sulfuric acid solution. Most of the copper ores treated by this process contain the minerals chalcocite (Cu_2S), covellite (CuS), or both. Copper from copper oxides ores can be extracted simply by leaching with sulfuric acid, so bioleaching is not necessary. Chalcopyrite ores ($CuFeS_2$) are very refractory, that is, the ore is very slowly oxidized by bacteria. Therefore, bioleaching of chalcopyrite ores has not been applied on a commercial basis. This represents an opportunity for biotechnology, because there are many low-grade deposits of chalcopyrite that have not been exploited because of lack of technology. Recommended approaches to the bioleaching of chalcopyrite are (a) use of thermophiles (*Acidianus* and *Sulfolobus* species), (b) design and implementation of new heap leach constructions to enhance bacterial activity through better oxygenation, and (c) development of bioreactors to bioleach copper concentrates (i.e., copper minerals that have been concentrated to remove useless rock). Because of the relatively low value of copper, novel concepts must be inexpensive.

Bioleaching using thiobacilli, the moderately thermophilic bacteria and the extreme thermophiles of the genus *Acidianus* and *Sulfolobus* can be applied to many sulfide-bearing ores including galena (PbS), sphalerite (ZnS), stibnite (Sb_2S_3), tetrahedrite ($Cu_{12}Sb_4S_{13}$), molybdenite (MoS_2), cobaltite (CoAsS), pentlandite [$(Fe, Ni)_9S_8$], and complex sulfide deposits containing several of these minerals [51]. There are no commercial applications for the bioleaching of any of these minerals. This is due primarily to (a) the importation of these metals from high-grade sources in other parts of the world, (b) the secondary production of these metals from other mineral processing (for example, the recovery of molybdenum during copper mining), (c) the refractory nature of some of these minerals that makes bioleaching difficult, and (d) the low market value of most of these metal commodities precluding implemention of techniques that increase production costs. Therefore, there has been little incentive to develop biotechnical processes for extraction of base metals other than copper. Technically, however, these base metal minerals could be leached using the same approaches described above for chalcopyrite.

3.5 Biotreatment of Fossil Fuels and Flue Gas

3.5.1 Coal Desulfurization. With the tightening of air quality regulations, decreasing sulfur dioxide emissions from coal-fired power plants has become increasingly important. Pre-combustion desulfurization is one method of cutting stack gas emissions.

Sulfur in coal occurs in three forms: (a) sulfate sulfur, (b) sulfide sulfur usually as pyrite or marcasite, and (c) organically bound sulfur present as dibenzothiophene, alkyl sulfides and thio groups in aromatic rings or attached to alkyl groups. Sulfate sulfur is readily removed by water washing of the coal. Sulfide sulfur, most of which is in particulate form, is removed by gravity separation. Oxidation by *Thiobacillus ferrooxidans* of finely dispersed inorganic sulfide minerals found in some coals has been researched for many years. Although technically feasible, no commercial plants using bacteria are in operation [52]. The technical and economic feasibility of bacterial removal of inorganic sulfide in coal was the subject of a 1988 study [53] and reviewed in 1990 [52].

The microbiological removal of organically bound sulfur is more complex than inorganic sulfur removal. Some bench-scale research was performed using the extremely thermophilic, acidophilic bacterium *Sulfolobus acidocaldarius* for extraction of sulfide sulfur and organically bound sulfur [54]. However, the effectiveness of this organism for extraction of organic sulfur is debatable. Bench-scale research continues using microorganisms for removal of organically bound sulfur [55,56]. Results of numerous studies on inorganic and organic sulfur biodesulfurization of coal, applications of genetics to coal biodesulfurization and bioreactor designs were reported at a 1992 Electric Power Research Institute/U.S. Department of Energy symposium [57].

Although considerable research has been performed on coal biodesulfurization, much research work remains before microbial technology could be considered ready for commercialization. Major technical limitations to commercial development appear to be (a) understanding and applying microbial processes for organic sulfur extraction, (b) development of bioreactors to handle high solids content for bioleaching inorganic sulfur, (c) potential effects of bioleaching/biodegradation on the characteristics (for example, Btu rating) of the coal, and (d) the need for downstream processing of substantial quantities of wastes from inorganic sulfur removal.

Although there appears to be a vast market opportunity for pre-combustion desulfurization of coal, examination of current practices at coal-fired power plants somewhat diminishes the potential opportunities. Some of these current practices include (a) continuing use in some instances of Grandfather clauses that contractually allow utilities to emit greater quantities of SO_2 than would be permissible for a newly constructed utility, (b) blending of low-sulfur western coals with the higher-sulfur coals of the eastern United States, (c) effectively removing sulfate sulfur and inorganic sulfur by washing and sink-float processes, respectively, to achieve regulatory sulfur levels, and (d) continuing reliance on stack-gas scrubbing methodology to remove SO_2. With air quality regulations currently at a cross-roads, however, other technologies, including biological processes, for pre-combustion desulfurization will probably receive greater attention.

Existing gravity separation and flotation processes for removal of inorganic sulfur seem preferable at this time to biotechnical processes that oxidize the sulfide to sulfuric acid. Development of large-scale plants for microbial desulfurization of inorganic sulfur could be severely limited by two factors [53, 57]: (a) the overwhelming technical obstacles relating to bioreactor design needed to enhance reaction kinetics, and (b) the substantial environmental and regulatory problems associated with generation and treatment of acid and metal-bearing wastes produced by the process. One bioprocess [58] augments the sink-float method of desulfurization by altering surface characteristics of either the coal or the pyrite/marcasite using thiobacilli. This alteration, which enhances flotation, merits attention, because it doesn't create the waste problem resulting from sulfide oxidation.

If biotechnology is considered for organic sulfur removal from coal, considerable research will be necessary to develop a technically viable process. Most researchers have thus far chosen to evaluate biological processes using synthetic substrates that have little in common with the real-world problem. Therefore, potential processes will require extensive testing on a variety of coals. Like pretreatment processes for refractory gold ores (see Sec. 3.2), coals from different deposits will respond differently to a developed process. Therefore, each biotechnical application will undoubtedly require considerable individual tailoring of the process.

A very thorough market analysis of the coal mining industry and the coal users should be performed to answer the questions: Who is the customer? What is the real market size? Where is the market (the coal fields or the users' facilities)? When will this market develop? How would biotechnology be implemented? Water use and water treatment issues are certain to play a critical role in where and how biotechnology is implemented.

3.5.2 Microbial Technology for Flue-Gas Desulfurization and Denitrification. The principal method for reducing sulfur emissions from the combustion of sulfur-containing coal is flue gas desulfurization. The most commercially important technology to achieve reduced sulfur emissions from stack gases is use of limestones and dolomites to adsorb acid gases. A significant waste disposal problem has developed in treating the large amounts of calcium sulfate (gypsum) produced from this flue gas desulfurization technology. Another problem is that, although a criteria pollutant for air emissions, oxides of nitrogen (NOx), are not removed by this desulfurization process.

Considerable research in the early 1980's was carried out by Cork [59] in conversion of SO_2 into elemental sulfur for the fertilizer industry. Cork's process entailed use of sulfate-reducing bacteria [14] to reduce the SO_2 in the flue gas to H_2S. Anaerobic photosynthetic bacteria converted the H_2S to elemental sulfur [59]. This process, however, did not address the NOx problem in flue gases. Other issues included the cost of providing the sulfate-reducing bacteria with a suitable organic energy source and the immensity of the reactor required to get sufficient light to the photosynthetic bacteria. Dasu and Sublette [60] have since proposed using the sulfate-reducing bacterium *Desulfovibrio desulfuricans* and the chemoautotroph *Thiobacillus denitrificans* to simultaneously remove the SO_2 and NO_x from stack gas emissions. The process concept involves using the sulfate-reducing bacteria to reduce SO_2, derived from regeneration of the alkaline adsorbents, to H_2S. T. denitrificans, which utilizes nitrate as an electron acceptor under anaerobic conditions, oxidizes the H_2S to elemental sulfur and reduces the NO_x in the stack gas to N_2 [60]. Other denitrifying bacteria have also been evaluated for NO_x removal [57]. For the integrated process using the sulfate-reducing bacteria, the high cost of feeding these heterotrophic bacteria remains an issue. Municipal sewage sludge and H_2 are being considered as low cost energy sources [57].

The opportunity to employ innovative processes to handle SO_2, NO_x and gypsum wastes will likely become greater with expanded use of high-sulfur coals, increased regulation of air emissions and reliance on scrubbers for removal of sulfur gases. Although there are promising new dry scrubbing processes that reduce NO_x to elemental nitrogen and remove SO_2 in stack gases, the SO_2 is released when the dry adsorbents are regenerated. Therefore, conversion of SO_2 to a useable product is still desirable and this represents an opportunity for biological sulfate reduction.

Any biotechnical developments to treat flue gases must include confirmation of the technical viability of the processes at bench- and field-scales, resolution of the expensive problem of feeding the sulfate-reducing bacteria, and improvements in bioreactor design to accommodate this technology.

3.5.3 Desulfurization of Petroleum. Heavy crude oils, oil shales and oil sands contain higher concentrations of sulfur than conventional crude oils. With world-wide depletion of conventional crudes there is greater use of heavy crudes. The higher sulfur content of these heavy crudes causes a variety of problems including corrosion, air pollution and the possibility of persistence in the environment of the organic sulfur compounds when oil spills occur. The organic sulfur compounds found in heavy crudes are like those associated with coal (aromatic and alkyl thiols, alkyl and cyclic sulfides, alkyl disulfides and thiophenes) [61,62]. Research on microbial degradation of these organic sulfur compounds has spanned several decades with little of practical value resulting. The dibenzothiophene gene has been closed and sequenced [57], which is an important first step in genetically altering microorganisms for selective attack on the organically-bound sulfur.

Much remains to be accomplished at a research level before commercialization of bioprocesses for petroleum desulfurization. At this time it would be premature to even speculate on business developments for biotechnology in this sector.

3.6 Biotechnology and Industrial Minerals

Biotechnology applications related to the industrial rocks and minerals sector have received scant attention. However, for the first time the use of industrial minerals in the field of biotechnology and the reverse—the existing and potential roles of biotechnology in industrial mineral mining and recovery—have been cataloged [63]. Industrial rocks and minerals are defined as non-metallic substances that are not mineral fuels. Table 119 is a partial listing of commodities considered to be industrial rocks and minerals. The industrial minerals' sector has the largest commodity production of all mineral categories. This is due to the greater numbers of products classified as industrial minerals as well as the commercial importance of certain industrial minerals (e.g., sand and gravel).

Table 119. Selected industrial minerals

Asbestos
Barite
Bauxite & alumina
Boron
Bromine
Cement
Chromite
Clays
Construction aggregates
Diatomite
Dimension stone
Evaporite & brine products
Feldspar, aplite, nepheline syenite
Fluorspar
Gallium & germanium
Garnet
Gemstones
Graphite
Gypsum
Helium
Industrial diamond
Kyanite
Lime
Lithium chemicals & minerals
Mica
Magnesite, magnesia
Nitrogen compounds
Peat
Perlite
Phosphate rock
Potash
Pumice
Rare earths
Sand & gravel
Silica sand
Soda ash
Sodium sulfate
Strontium
Sulfur
Talc
Titanium
Vermiculite
Zeolites
Zircon

Opportunities for biotechnology in the industrial mineral and rock sector include (a) silicate degradation for aluminum recovery, (b) phosphate solubilization, (c) inhibition of biocorrosion of natural stone and man-made constructions, (d) surface modifications of materials for improved ceramic properties, (e) beneficiation processes to remove contaminants from certain industrial minerals, and (f) solubilization of rare earth elements.

The primary source of aluminum is bauxite, which is imported to the United States. The United States and Europe do have large deposits of aluminosilicates, which could serve as sources of aluminum.

However, owing to the high energy requirements of proposed extractive processes, these deposits have not been exploited [51]. Fungi and certain bacteria have been evaluated for their ability to degrade the crystal lattices of aluminosilicates and silicates releasing aluminum [51]. All of these organisms are heterotrophic, producing either organic acids that attack the rock or complexing agents that react with certain constituents of the rock lattice. Much basic research must be undertaken to identify mechanisms for aluminum beneficiation and to optimize processes before any field trials are initiated. Because these organisms are heterotrophic, an affordable organic energy source is a serious consideration in developing a commercially viable biotechnical process. Important to a venture exploiting this technology is understanding market aspects of bauxite importation.

Acid solubilization of phosphate to produce fertilizers is a well-defined process. Research has been carried out using acid generated by species of *Thiobacillus* oxidizing sulfur-containing minerals [64]. Additional work is underway evaluating phosphate solubilization by other microorganisms [62]. Biotechnical processes my be applicable in recovering phosphate lost to mineral wastes generated during processing. Biotechnical applications, however, must be economically compared with the conventional use of sulfuric acid for phosphatic fertilizer production.

Clearly one of the most important commercial opportunities for biotechnology in the industrial mineral/rock sector is a process to inhibit the degradation of natural stone and constructions made from industrial rocks and minerals. Microorganisms belonging to the genus *Thiobacillus* develop on stone and concrete when reduced sulfur compounds are available. Methylmercaptan, H_2S, and thiosulfate present in concrete sewage works, can serve as energy sources for these organisms [65]. These organisms catalyze the production of sulfuric acid and accelerate corrosion by a factor of eight times over abiotic conditions. Because of increased sulfur compounds in the atmosphere from the burning of fossil fuels, acid rain tends to create slightly acidic conditions on stoneworks. These conditions are optimum for development of thiobacilli which enhance pitting and corrosion of these works. Many other microorganisms also colonize building stone [62] resulting in severe corrosion. Products or processes to inhibit microbially-induced corrosion are needed.

The extraction of iron from silica and clays by fungi, such as *Aspergillus niger* that produces an organic acid, has been demonstrated [66]. This activity has important implications in the beneficiation of ceramics. Little research into the microbial extraction of rare earth elements has been reported. Glombitza et al. [67], however, reported bioleaching of lanthanum, cerium, praseodymium and other heavier rare earth elements from zircon mineral using *Thiobacillus ferrooxidans* and *Acetobacter* species. The mechanism used by this consortium of microorganisms was not defined in this study.

Biotechnology to extract or beneficiate industrial minerals and to prevent biodeterioration of structures made from industrial rocks and minerals has received so little attention that much basic research remains before commercial practices are considered. The most lucrative opportunity would appear to be the prevention of biodeterioration of concrete and stoneworks.

3.7 Leaching of Uranium

The bioleaching of sulfur- and iron-containing uranium ores is the second largest application of biotechnology in the mining industry next to the bioleaching of low-grade, sulfidic copper ores. Uranium bioleaching has been applied successfully throughout the world for extraction of uranium from operations that have previously been mined by conventional processing. Two successful practices have been commercially employed [68]. One practice involves the spraying of underground excavations with water, allowing bacteria to oxidize the sulfur and iron minerals, and then re-spraying the excavations with water to wash the solubilized uranium to sumps for recovery. The other practice involves flooding of underground excavations with water, allowing the bacteria to oxidize the uranium-bearing minerals, and recovering the uranium values.

Little research on biological uranium leaching is carried out today and few commercial applications are practiced, because of poor market conditions for uranium. Unless nuclear power is revitalized, little opportunity exists for biotechnology in this industrial sector.

4.0 Guidelines for Introducing Biotechnology to the Mining Sector: Getting Started and Avoiding Pitfalls

This chapter has summarized a host of potential opportunities for application of biotechnology throughout sectors of the mining industry. Environmental control, precious metal mining and corrosion control of concrete and stoneworks offer the greatest immediate market potential. The applicable biotechnologies are as disparate as the areas of mining to which they can potentially be applied. No single individual or company could expect to be an expert in all of these possible biotechnical applications. Because of the cross-disciplinary nature and sheer extent of the opportunities introduced in the chapter, two questions must be answered:

- How does a fledgling biotechnology company with a creative idea for the mining sector introduce technology to the industry?
- What pitfalls should be avoided in introducing technology to mining?

As expected most biotechnology companies are managed and staffed by scientists and engineers from universities, the biotechnology industry or both. These entrepreneurs have little practical knowledge of the mining industry. The first step for the biotechnology company is to bridge the knowledge gap between pure biotechnology and mining practices. This can be accomplished by reading biotechnology and mining journals that publish articles in the area and by attending trade society meetings in mining and biohydrometallurgy.

Geomicrobiology Journal, *Biotechnology and Bioengineering*, *Journal of Industrial Microbiology*, and *Applied and Environmental Microbiology* are among professional journals that publish scholarly articles relating to biotechnology applications in mining. These articles, largely written by biotechnologists, tend to be research oriented as opposed to applied. On the other hand, several journals, including *Mining Engineering* and *Journal of Metals*, which serve the mining industry, occasionally publish articles related to biotechnology. These articles tend to be more operations oriented. All of these publications are important in providing the start-up biotechnology firm with a balanced view of the scope of applications and technologies.

The International Biohydrometallurgy Symposium held every other year is an excellent forum to obtain basic and applied information from university and industrial scientists and engineers. These meetings also provide a good opportunity to meet researchers as well as potential users of the technology. The Society of Minerals, Metals and Materials (Warrensdale, PA) and the Society of Mining Engineers (Littleton, CO), professional societies serving the mining industry, sponsor annual meetings that usually include multiple sessions on biotechnology applications in mining. Most often talks in these sessions are presented by researchers as opposed to users, but the talks are well attended by the mining industry. Attending these meetings provides ample opportunity to meet and talk to researchers and potential users of biotechnology.

The most important step in introducing biotechnology to the mining industry is obtaining specifics about the market opportunity to prepare business and market plans. In fact the best course of action is to find a problem with a large market opportunity that can be solved using biotechnology, then develop the technology around the market opportunity. It is generally a mistake to develop a product or process, then try to find a market for the technology. Specific market information is usually only available through mining industry insiders. Approaches to accessing this information include establishing joint ventures, obtaining venture capital, using advisors, and/or hiring experts.

Joint ventures provide not only needed capital to start-up biotechnology firms, but can be sources of insider information and can yield marketing partners. Joint ventures between early stage biotechnology firms and mining companies are rare, because, unlike the pharmaceutical and health care industries, the mining industry has no precedence for such alliances. However, joint ventures between engineering and construction firms that service the mining industry have been established. The biotechnology firm in search of a value-added partner should look into liaisons with vendors to the mining industry. These vendors not only have intimate knowledge about mining, but have long-established working relationships with many mining companies. Business and marketing relationships with engineering/construction firms could mitigate some difficult business issues between biotechnology and mining companies that were noted in Section 3.2.4.

Venture capital firms are not only a source of capital, but can be a source of needed industry information. If this route for capitalization is selected, the biotechnology company should carefully select venture capitalists that have an excellent network of contacts within the mining industry. These contacts can be readily accessed through introductions by the venture capital investor.

Hiring an expert from the mining industry is an obvious alternative, however, this may be a luxury that a start-up biotechnology firm can ill afford. Usually the time at which a start-up company needs market specifics doesn't coincide with the time the company can adequately compensate an individual with such expertise. Furthermore, the expertise of that individual may not be needed a short time later. He/she may not have other expertise, such as engineering skills, that are needed by the company at a later time. Also, the market analysis may indicate an insufficient market opportunity, necessitating a lay-off. Advisory boards, which include mining industry representatives that can be consulted about business strategies and market opportunities, may be a more cost effect route for a start-up biotechnology organization. Advisory board members can often be compensated in part with stock options rather than cash.

For some biotechnology products and processes the question of what to sell is not trivial. If the product is microorganisms, once these organisms are established in the system no further sales will be made. If the product is a reagent produced by a microorganism, this reagent can be packaged and sold like other chemical reagents. Considerable thought and background knowledge about how other technologies are sold to the mining industry needs to be gained before negotiating for royalties, service fees, etc. is initiated. Other guidelines and strategies for introducing biotechnology to the mining industry were included in sections relating to specific market opportunities.

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Bioremediation and Environmental Control Technology

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Use of microorganisms for treatment of wastes and remediation of hazardous waste sites is increasing rapidly. New discoveries in the biological sciences will feed continued growth of this field. Several key research areas are described in this chapter, and their applications to biotreatment are outlined. A strategy for identification of new applications is outlined, based on utilization of inherent strengths and capabilities of microorganisms. The current emphasis on waste minimization suggests that biotreatment of newly generated waste has limited potential. However, bioremediation of hazardous waste sites, coupled to advantage with other physico-chemical technologies, has great potential.

Key words: biodegradation; bioremediation; biotreatment; environmental control technology; hazardous waste sites; microorganisms; waste treatment.

1. Introduction

The engineered use of microorganisms to treat wastes is increasing. Significant reasons for this increase include societal pressures to treat wastes more thoroughly, improved performance of bioprocesses arising from better scientific understanding, and societal and technical limitations of alternative technologies. These reasons will likely continue to favor increased use of microbial-based technologies, particularly if the many recent advances in biology can be translated into technological applications.

The goal of this chapter is to introduce opportunities and needs for technical advances in biotreatment of wastes that could lead to new business ventures. The approach will be first to lay out the fundamental principles and concepts upon which biotreatment is based. From this foundation, several "cutting edge" areas will be described. No attempt will be made to imply what can and cannot be done. It is well known that ignorance of conventional wisdom on what cannot be done is often helpful when it comes to finding innovative solutions to problems.

1.1 Why Biotreatment?

For this discussion, biotreatment, biodegradation, and similar terms refer to the biochemical transformation of contaminants and wastes by intact microorganisms. The majority of biochemical transformations involve oxidative and reductive changes to organic chemicals. However, inorganics such as sulfides, nitrates, certain metals, and other species can be biotransformed and/or sorbed by microorganisms.

Engineered bioprocesses offer several advantages relative to alternative waste treatment technologies:

- Biodegradation is a "natural" phenomenon, which contributes to societal acceptance;
- Biodegradation is usually a destructive process (nature's incinerator), which is generally preferable to technologies that immobilize the wastes and/or perhaps simply transfer the wastes to another media (e.g., liquid to solid) or another location;

- Biodegradation occurs at near-ambient conditions, which minimizes energy and equipment requirements;
- Biodegradation can be used selectively to target destruction of contaminants without destruction of total organic content; and
- Biotreatment is often (but not always) less costly than other technologies to achieve acceptable treatment.

1.2 Waste Characteristics

Waste streams that are typically suitable for biotreatment have relatively dilute concentrations of organics, and may contain a variety of different organic chemicals. Higher concentrations of many (but not all) organics are toxic or inhibitory to microbial activity; furthermore, nonbiological treatment technologies are often more economical for concentrated streams. Each waste stream is a special case. Hidden in these circumstances is an opportunity: Means to mitigate the adverse effects of high concentrations of organics will extend the applicability of biotreatment to more waste streams. The need to biodegrade mixtures of organic chemicals also presents special problems (and opportunities). More will be said later about this issue.

2. Current Practice

Many publications contain information on current practice in biotreatment of wastes and bioremediation. The bibliography at the end of this chapter contains suggested introductory and overview journal articles, books, and reports that cover principles and current practice. Also included are several periodicals that should be monitored regularly to keep abreast of new developments. These sources will provide much more detailed information on current practice to supplement the general overview given in this chapter. These sources will also provide the background and basis for the technical needs and opportunities discussed later in this chapter.

It is helpful to divide current practice into two broad categories: Biotreatment of waste streams generated by current activities; and bioremediation of sites contaminated as a result of previous activities (which may include inadequate previous treatment of wastes). These two categories present different opportunities and challenges for the use of bioprocess technologies.

2.1 Environmental Control Technology

Treatment of wastes streams generated by current activities is often called environmental control (or pollution control). Biotreatment of aqueous waste streams is present practice, of course. Many municipalities and industrial facilities have activated sludge or trickle filter plants for aerobic (oxidative) waste water treatment. The biosludge from these operations, which consists of excess microorganisms, can be stabilized by anaerobic digestion. Biotreatment may also be carried out in lagoons. Bioreactor systems are available for anaerobic treatment of wastewater and recovery of methane for fuel.

There are undoubtedly opportunities for process improvements in these technologies. However, it can be argued that effective waste minimization practices will lead to less waste to be treated, with less economic impact. Therefore, technological improvements in bioprocesses for waste treatment may have limited impact. Nevertheless, some of the technical opportunities discussed below, such as sensors and analytical techniques, may be applicable to biotreatment of currently generated waste streams. Waste minimization activities may also lead to generation of dilute waste streams that are good candidates for biological treatment.

2.2 Bioremediation

Remediation of contaminated, previously used sites presents different challenges. Contamination may be present in soils and sludges as well as water—and in subsurface locations where accessibility is the major hurdle. Bioremediation is often a leading candidate for cleanup of these sites, in part because alternative technologies are often infeasible (i.e., prohibitively expensive). Improvements in bioprocess performance for bioremediation are likely to enjoy widespread and rapid implementation and to provide substantial economic savings.

Bioremediation of selected types of sites is now commercial practice. Petroleum hydrocarbon spills and leaks from fuel storage tanks are frequently treated by bioremediation, provided that the contamination is accessible. Other relatively simple chemicals, such as formaldehyde, acetone, benzene, glycerol, etc., can be biodegraded relatively easily. Surface contamination can be treated by landfarming techniques—simply addition of nutrients and tilling to provide aeration for biooxidation. If the contamination is at a shallow depth (for example, a leaking fuel tank), nutrients and oxygen may be added by installing a well field and pumping water into and/or out of the contamination area. The hydrological characteristics of the site are obviously critical to successful delivery of nutrients.

In addition to in situ bioremediation described above, contaminated soils and water can be treated in various types of bioreactors. Soils are amenable to aqueous slurry reactors, with addition of nutrients and appropriate inocula of microorganisms (perhaps those already present in the soil). Contaminated water is frequently treated in immobilized-cell bioreactors, such as a trickle-filter or packed-bed bioreactor. The water may be drawn from lagoons, pumped from wells, etc. There is a substantial published literature covering these types of systems, and numerous vendors and contractors provide these technologies.

Situations to which bioremediation has not yet been successfully applied usually are characterized by difficult-to-degrade contaminants and/or inaccessibility of the contaminated zone. The former includes many chlorinated solvents and nitrogen- and sulfur-containing organic chemicals. The contaminated zone may be effectively inaccessible in the short term because of the local geology and hydrology. If the contaminated zone has been created by seepage and slow movement over many years, it may be very difficult to introduce nutrients and oxygen throughout the zone in a short amount of time.

An additional factor which may make a site unsuitable for bioremediation is the presence of chemicals toxic to the microorganisms. Usually this is a concentration-dependent effect. “Low” concentrations of most anything will not be a problem, whereas “high” concentrations of many chemicals will inhibit biodegradation. Laboratory treatability studies are used to investigate this issue before a full-scale bioremediation is implemented.

3. Requirements for Successful Bioremediation

As a prelude to discussion of development needs and opportunities, consider first the general requirements for a successful bioremediation process. For above-ground bioreactor technologies, the two primary requirements are that satisfactory conditions be established for biodegradation activity by the microorganisms, and that adequate contacting exists between the microorganisms and the contaminants to be degraded. There are many ways to meet these requirements; thus there are opportunities for process optimization with respect to cost and technical performance.

Satisfactory conditions for bioactivity include many factors: pH; temperature; chemical nutrients including phosphorus, nitrogen, trace metals; absence of inhibitors; and an appropriate microbial population. Generally speaking, different species of microorganisms may require slightly different conditions for optimal biodegradation activity, and will prefer to attack different types of contaminants. This is the realm of the microbiologist, whose expertise and collaboration are invaluable.

Adequate contacting between the microorganisms and the contaminant is essentially a mass transfer problem. A high surface area of microorganisms is usually desirable; individual microbial cells in suspension are good, but the cells tend to wash out of the reactor and the bioactivity is lost. For this reason, various types of immobilized-cell reactors are popular. Each has its advantages and disadvantages for particular applications. Opportunities exist for clever solutions to the mass transfer problem while maintaining high levels of bioactivity in the bioreactor.

The requirements for in situ bioremediation of contaminated soils, lagoons, and groundwater are similar, but more difficult to accomplish. Usually, indigenous microorganisms are induced to do the task. It has been found that most (but not all) contaminated sites already contain microorganisms capable of degrading the contaminants. So why is the site still contaminated? Because other necessary conditions for microbial degradation activity are not present (see above). The technical challenge, then, is to find a way to alter the conditions at the site (such as pH, nutrients, oxygen) to allow the indigenous microbial populations to express their latent biodegradation activities. In addition to knowledge about the microbial populations, it is usually necessary to understand and control (to some extent) the hydrological and geochemical phenomena.

Occasionally, it may be possible to introduce new microorganisms into soils, lagoons, and confined subsurface aquifers. However, the utility of doing so is often marginal. An increase in bioactivity may be achieved for a short time, but the new microorganisms rarely seem to survive in adequate numbers to achieve a long-term, permanent effect. Development of new means to enhance their survival and bioactivity could improve process performance, but also may increase regulatory scrutiny.

Genetically engineered microorganisms will someday be used in bioremediation processes. Aggressive companies are developing technologies now in anticipation of a more favorable regulatory environment. Use of these organisms may depend on even more careful attention to the "requirements" described above, since genetically engineered organisms tend to be somewhat fragile. But more rugged organisms will probably be developed.

4. Building a Better Biotreatment Mousetrap

An attractive strategy for creation of better (more competitive) biotreatment technologies is to capitalize on the inherent strengths of microorganisms. Biotreatment will not be the answer to all remediation needs; forget applications for which microorganisms seem to have no natural propensity, and focus on areas of inherent strength, such as:

- uptake of chemicals at dilute concentrations;
- operation at ambient temperatures and neutral pH;
- selective degradation of certain chemicals while having no effect on other chemicals;
- self-replicating and self-maintaining;
- capacity to grow, propagate, colonize;
- potential for genetic engineering; and others.

A second important—perhaps critical—consideration is the inter- and multidisciplinary nature of biotechnology. Clever and innovative applications are likely to arise from nitty-gritty collaboration among technical people with differing disciplinary expertise, yet who have a willingness to accommodate foreign concepts from different disciplines.

5. The Cutting Edge

The following topics are active research areas at universities and other research institutions, and are likely breeding grounds for new development opportunities.

5.1 Cometabolism

Cometabolism, sometimes called fortuitous metabolism, is the degradation of chemicals that are not providing energy or other benefit to the microorganisms. Simultaneously, the microorganisms are deriving energy and other necessities from the metabolism of completely different chemicals. This phenomenon occurs, in part, because of the non-specificity of some enzymes in the metabolic pathways. Enzymes that are necessary for metabolism of the primary energy source may also catalyze degradation of other compounds, even though the microorganisms apparently derive no benefit from these latter reactions—hence the designation "fortuitous metabolism."

Some chlorinated organics are among the chemicals that can be degraded by cometabolism. Chlorinated organics, such as trichloroethylene, are not normally primary substrates for microorganisms; insufficient energy is obtained, dealing with the chlorine is energetically difficult, and these chemicals are frequently toxic at modest concentrations.

Cometabolism is the basis for new bioremediation processes for contaminated soils and waters. Microorganisms are stimulated with nutrients and a primary substrate for carbon and energy. As the primary substrate is metabolized, the contaminants are cometabolized. However, process control and performance can be difficult to manage because of the fortuitous nature of the desired reactions. Degradation of the contaminants appears to be only indirectly influenced by parameters that are normally used to control bioprocesses.

One example of a technology under development is cometabolism of trichloroethylene (TCE) by methanotrophs (methane-utilizing microorganisms). The enzyme methane monooxygenase is utilized by methanotrophs to oxidize methane for energy. It also catalyzes the formation of TCE epoxide, which then spontaneously hydrolyzes to form other species that are readily biodegradable to carbon dioxide, water, and chloride. Bioreactor-based processes are being developed and demonstrated for remediation of groundwater contaminated with TCE. Other investigators are experimenting with in situ versions of the cometabolic concept.

The basic appeal of cometabolism is that it offer pathways for degradation of chemicals that are not normally substrates for microorganisms. Thus the catalog of contaminants that can be handled by bioremediation could be substantially increased. It is likely that microbiological studies will continue to reveal new instances of cometabolism. Applications to remediation will require clever approaches to harness this "fortuitous" behavior.

5.2 Mixtures of Substrates

Mixtures of substrates are commonly encountered in waste treatment and remediation. This condition occurs because historically a variety of wastes were managed in the same manner. For example, several waste streams would be pumped to a common lagoon or pit. Leachates from waste disposal sites are obviously influenced by whatever was placed at the sites.

Microbial cultures degrade mixtures of substrates in complex and unpredictable ways. The normal mode of action of microorganisms is to degrade one substrate at a time, starting with the most easily utilized compound. When this substrate is gone, the microorganisms adjust their metabolism to tackle another substrate. However, enzymes and metabolic pathways are not perfectly selective, and simultaneous utilization of several substrates may occur. Furthermore, different species of microorganisms in mixed cultures will exhibit different substrate preferences, which might lead to advantageous simultaneous metabolism of multiple substrates.

The various interactions and relationships for mixtures of substrates are generally not understood adequately to be useful in design and operation of bioprocesses. To compensate for this lack of detailed understanding, conventional biotreatment processes such as activated sludge are designed extremely conservatively to assure adequate performance.

There is much room for improvement in bioprocesses if clever means can be found to deal with the uncertainties associated with mixtures of contaminants and mixed microbial cultures. One approach, for example, is to separate the overall treatment process spatially in order to permit a variety of different operating conditions. This configuration is sometimes called a stagewise process. A recent example is the sequencing batch reactor concept, which is being used successfully for biotreatment of hazardous waste leachates.

5.3 Adaptation to New Environments

Adaptation to new environments is a significant characteristic of microorganisms. A modest amount of information is available on the response of microorganisms to various types of stress. For example, deprivation of substrate induces some microbial species to increase production of extracellular polysaccharides, which are the "glue" for biofilms. This response is thought to aid the survival of the population when the reproductive capacity is reduced in the absence of substrate.

Cells in a newly-forming biofilm will multiply until the surface of the support matrix is covered and a critical film thickness is reached (controlled in part by diffusion of substrate into the biofilm). At this point the growth rate of the culture may decrease substantially, while the metabolic processes are maintained for degradation of contaminants. This behavior is an example of a natural response to a different environment (biofilm compared to suspended growth) that is advantageous for bioprocesses because the unwanted production of microbial biomass is minimized.

The response of microbial cultures to changes in the concentrations of trace nutrients, such as metals, may be significant for better or worse. Temperature and pH are well-known parameters that affect the behavior of microorganisms. However, typically only the growth rate and the substrate degradation rate are considered. Do temperature and pH (and other variables) affect the behavior of microorganisms in other more subtle ways that could be used to advantage to improve process performance and develop new technologies?

5.4 Biosorption

Biosorption is a potentially useful phenomenon for waste treatment and environmental remediation. Heavy metals and radionuclides may be physically sorbed by microbial cells without undergoing any chemical reactions. The sorption may be both intracellular and extracellular. High loadings are achievable. In some cases, the sorption is reversible and the metals can be recovered. Metabolic activity is not necessary; resting cells and non-viable cells can show sorption activity. Significant variability is seen in sorption capability among microbial species.

Several private sector companies are offering biosorption-based technologies. However, biosorption is not yet widely used. One approach that might offer a niche for increased application might be to couple biosorption with other functions of the microorganisms to create bioprocesses in which the microorganisms serve a dual purpose.

5.5 Metal Redox Reactions

Metal redox reactions are a relative newcomer to biotreatment. The oxidation state of some metals can be altered by biochemical reactions. Two notable examples are methylation of mercury (and the reverse demethylation) and chromium VI to chromium III. Changes in the oxidation state may alter the toxicity of the metal and its environmental fate. Accompanying changes in the physico-chemical properties, such as solubility, may provide the basis for new biotreatment processes.

5.6 Immobilized-Cell Bioreactors

Immobilized-cell bioreactors are rapidly replacing suspended-growth systems as the configuration of choice for many applications. The principal advantages include inherent retention of the microbial catalyst within the bioreactor, high microbial cell loadings for high reaction rates, and improved resistance to shock and process upsets.

A wide variety of immobilization techniques have been proposed, tested, and in some cases implemented at significant scale. The principal remediation applications have been to contaminated groundwater and other leachates and wastewaters using variations of packed-bed bioreactors containing biofilms. Soil slurry bioreactors could be considered immobilized-cell bioreactors since the microbial populations adhere to the soil particles as well as exist in suspension in the aqueous phase.

Experience has shown that many natural microbial populations will form biofilms and adhere to solid surfaces provided for this purpose. Means to promote film formation and to influence the characteristics of the films are being sought, with some modest successes to date. Perhaps not surprisingly, some types of surfaces appear to be more suitable for biofilms than others.

Biofilms show variable resistance to colonization by unwanted microorganisms present in the waste stream. Can a biofilm of a pure culture (single microbial species) be maintained in an unsterilized environment? The findings and techniques arising from research on these types of issues are likely to lead to expanded remediation applications and improved process performance. An example is the recent interest in gas-phase bioreactors as an approach to isolate pure microbial cultures from unsterile liquids.

Immobilization is not limited to biofilms. Another popular mode is biobeads consisting of a support matrix, such as alginate or carrageenan, to which the desired microorganisms are added. The biobeads are usually relatively small to minimize mass transfer (diffusional) effects. Properties of the biobeads can be altered in many ways to achieve desirable characteristics to improve process performance and operability.

5.7 Mixed Microbial Cultures

Mixed microbial cultures are nature's way—naturally occurring populations of a single microbial species are rare. Mixtures of different microbial species with different metabolic capabilities exhibit a variety of synergistic phenomena that favor survival. For example, metabolic intermediates formed by one species may be ideal substrates for other species. Classical biotreatment of wastewater works on this basis. Individual microbial species with the unique degradation capabilities may comprise only a very small fraction of the total microbial population.

Many complex interactions influence the detailed makeup of mixed cultures. Obviously, the nature of the organic carbon and energy source and the nutrients will be important; methanotrophs will not be active when there is no methane. The relative growth rates of different species and the rates at which they consume substrate(s) appear to be significant. There is considerable question as to whether there is a single "unique" mixed population that corresponds to a particular set of substrate and other environmental conditions. Rather, the system may exhibit multiple steady states, so to speak. Is the concept of pseudo-steady state a meaningful model?

When the behavior of mixed cultures is better understood, perhaps it will be feasible to design and construct stable mixed cultures having specified capabilities for particular remediation applications. In the meantime, improvements in the ability to control and manipulate mixed cultures may open up new and improved bioprocess applications.

5.8 Contacting Methods

Contacting methods are one of the keys to successful bioprocesses. Although the concept sounds obvious and trivial, it is absolutely necessary that the contaminants and the microorganisms be brought into intimate contact in order for biodegradation to occur. The effectiveness and efficiency (and economics) of bioprocesses are directly influenced by how well this contacting is achieved.

The function of the bioreactor is to provide a contacting means and a local environment conducive to biodegradation. Desirable goals often include high microbial cell concentrations for high degradation rates, and minimal residence time of the media being treated in order to minimize equipment sizes.

The overall rate at which a bioreactor is able to degrade contaminants is governed by the rates of the individual mass transfer (diffusion) and chemical reaction steps. Usually one of the individual steps will be significantly slower than the others. This step effectively determines the overall rate for the bioreactor. If clever means can be found to increase the rate of this slowest, rate-determining step, then the overall kinetic performance of the bioreactor can be improved. The identity of the rate-limiting step will depend on the type of bioreactor and the type of application.

Similar principles and arguments apply to in situ bioremediation. Good contacting is still critical, but may be much more difficult to achieve. It is sometimes conceptually useful to consider the entire in situ site to be a bioreactor. Can this bioreactor be stirred? Mixed? How can fluid flow be accomplished for delivery of nutrients? Is uniform fluid flow desirable? Possible? Is there another way to provide nutrients throughout the bioreactor? Is it necessary to remove reaction products from the bioreactor? Significant advances in in situ bioremediation can be achieved through clever approaches to issues such as these.

5.9 Dynamic Characteristics

Dynamic characteristics of microorganisms offer yet another route to potential performance improvements and new processes. Because of the complex network of series and parallel reactions that comprise metabolic pathways, the dynamic behavior with time can be complex and potentially useful. Furthermore, add to these characteristics the species interactions in mixed cultures. It is doubtful if steady state is ever actually established, even though steady-state models are useful representations for engineering purposes.

For example, consider the cometabolism of TCE by methanotrophs, which was described earlier. Both methane and TCE compete for the active site on the enzyme; as a result, TCE degradation should be better at lower methane concentrations. It has been observed that TCE degradation can also be improved temporarily by removing methane and adding formate as the reductant. The effect is short-lived, however, probably because TCE is a toxicant to the enzyme and in the absence of methane the key enzyme, methane monooxygenase, is no longer synthesized by the cells. Thus it is necessary to add methane periodically to maintain the enzyme for TCE degradation. Can methane and formate pulsing be used to improve process performance? Pulsing is also being investigated to reduce plugging of groundwater aquifers by excessive growth of microorganisms near injection wells.

Batch processes are inherently unsteady state, and have been used historically to take advantage of the time-varying characteristics of cultures, especially in the pharmaceutical industry. Site remediation can also be considered a batch process; there is a starting time with initial conditions, followed by a period of change toward an acceptable final condition, at which time the process is complete. Perhaps there are opportunities to take advantage of the dynamic behavior of microorganisms in new ways.

It was mentioned earlier that the microbial species with the degradation capabilities of interest may comprise only a small fraction of the total population. What can be done to increase these microorganisms without investing carbon and energy in the growth of other more numerous organisms that do not contribute to the degradation activity? Can engineered approaches be developed, or are we at the mercy of the natural microbial population dynamics?

5.10 Integrated Processes

It is not necessary nor perhaps even desirable that biotreatment be the only technology brought to bear on a particular problem. Biotreatment can often be a component of a multistep treatment process. Consideration of the unique strengths and capabilities of microorganisms will help to identify new applications.

5.11 Analytical Methods

Analytical methods with improved sensitivity, selectivity, and robustness are always welcome. Microorganisms offer opportunities to create new methods based on the characteristics of the microorganisms. A prime example is the spate of new diagnostic techniques in human and animal health care based on antigenic behaviors. Many of these advances will be transferrable to environmental applications. Methods that are rapid and rugged for field use are especially desirable, as are techniques that are minimally invasive and/or destructive.

Improved rapid capabilities to assess the condition of microorganisms will lead to improved process performance. It would be nice to know that the microbial population is failing before a laborious series of chemical assays of contaminant concentrations shows that the rate of degradation has decreased.

6. Market Potential and Position

Several studies have been done to estimate the market potential for biotechnologies applicable to waste treatment and environmental remediation. This author has no reason to favor the analysis of one study over another. One recent study reported that the current waste biotechnology market is $800 million per year, and will grow 30% per year. Other sources of information on market projections are identified in the Bibliography.

The U.S. Environmental Protection Agency (EPA) compiles information on sites needing remediation and current activities in site remediation. Sites that have been determined by the EPA to need remediation are placed on the National Priority List (NPL); this list is updated periodically. The EPA Bioremediation Field Initiative is a program to provide information on the application of bioremediation technologies (see Bibliography). EPA also publishes a summary of the application of innovative treatment technologies, including biotechnology (see Bibliography). This latter report helps to indicate how bioremediation is faring in competition with alternative innovative technologies. Periodic updates are issued.

Processes that use microorganisms are patentable; most current bioremediation technologies are covered by one or more patents or licenses. Patents can also be obtained for particular microorganisms. Check with an experienced patent attorney.

For NPL sites, implementation of a particular remediation technology is subject to review and approval by the EPA. A formal procedure for this review and approval is specified. It may be possible to remediate sites not on the NPL without advance approval by the EPA. However, advice should be sought from persons experienced in dealing with the regulatory community.

7. Technology Development and Implementation

Successful development and implementation of new biotreatment technologies requires three broad categories of expertise:

- Microbiology
- Process engineering
- Regulatory constraints

Assistance should be obtained from experienced persons; these areas are too complex to be handled adequately by technical laypersons.

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